



**INDIAN MEDICAL ASSOCIATION
ACADEMY OF MEDICAL SPECIALITIES
(IMA AMS)**

Head Quarters, Hyderabad, Telangana

**Annals 2022
National AMSCON**

**Theme :
Medical Emergencies**

**November 5-6, 2022
Kolkata, West Bengal**



**IMA ACADEMY OF MEDICAL SPECIALITIES
Head Quarters, Hyderabad, Telangana**
4-5-357, 2nd Floor, IMA Building, Koti, Esamia Bazar,
Hyderabad 500 027 | Tel : +91 40 24740015
E-mail : imaamshyd@gmail.com | www.ima-ams.org

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IMA AMS Hqrs



Dr. Srirang Abkari
Hon. Editor (Annals),
IMA AMS Hqrs



INDIAN MEDICAL ASSOCIATION ACADEMY OF MEDICAL SPECIALITIES

Annual Journal of National AMSCON - 2022

November 5-6, 2022
KOLKATA

Dr. G. N. Prabhakara
Chairman, IMA AMS

Dr. Sanjeev Singh Yadav
Hony. Secretary, IMA AMS

Dr. Srirang Abkari
Hony. Editor, IMA AMS

Dr. Sahajanand PD Singh
National President, IMA

Dr. Jayesh M. Lele
Hony. Secretary General

Dr. Anil Goyal
Hon Finance Secretary, IMA



IMA PRAYER



May everybody be happy
May everybody be healthy
May everybody be free from pain
May everybody be free from sorrow
May we be the healing cure
Beyond every greed & lure

FLAG SALUTATION

We, the members of Indian Medical Association
Stand here to salute our National Flag.
Its honour and glory shall be our light and strength
And its course shall be our course.
We pledge our allegiance to it and realizing our responsibilities
As the accredited members of this National organization,
We swear we will dedicate everything in our power
To see it fly high in the comity of Nations.
Jai Hind!

As the Covid-19 pandemic wanes, we have decided to refocus on the traditional medical problems faced by us in our daily clinical practice. Therefore the theme for this issue of the Annals was chosen as "**Medical Emergencies.**" While the words of Arnold H. Glasow - "*One of the tests of leadership is the ability to recognize a problem before it becomes an emergency*"- are very true, *we as leaders in our work place have to manage many medical emergencies. And the best way to handle them is to be prepared. I would like to quote Theodore Roosevelt who said "Make preparations in advance, you never have trouble if you are prepared for it" And as Max Mayfield said "Preparation through education is less costly than learning through tragedy"*



This issue of Annals aims to prepare medical professionals to handle common medical emergencies. I am extremely thankful to the eminent authors who have spared their valuable time and contributed articles for this issue. I am sure their rich experience and expertise in their respective fields will enrich the knowledge of all the readers in handling emergencies.

We need to remember that the patient is at the center-stage of our medical world and we owe our very existence to him / her. Having realized this, we must work untiringly to alleviate their sufferings and through a combination of clinical examination and appropriate investigations fulfill our responsibility.

As we celebrate the 75 years of India's Independence, medicine is one entity which unites us all, transgressing all the boundaries of different states, religion, caste, creed and economic strata. We all have but one aim in view to help a patient get better and I truly salute all the medical professional of my country for their dedication and sacrifice.

I pay my tribute to Sir William Osler and would like to quote him- "*The practice of medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head. Often the best part of your work will have nothing to do with potions and powders, but with the exercise of an influence of the strong upon the weak, of the righteous upon the wicked, of the wise upon the foolish.*"

It has been a wonderful experience to serve the IMA AMS in the capacity of its Honorary Editor and I am grateful to guidance and encouragement of our Patron and visionary leader Dr. Ketan Desai. My sincere thanks to Dr. Sahajanand Prasad Singh, National President, IMA for his words of wisdom and inspiration, Dr. Jayesh Lele, Honorary Secretary General, IMA for the support and stimulus to excel in academics, Dr. E. Ravindra Reddy, National Vice-President for his infectious passion for maintaining ethics in Medicine, Dr. GN Prabhakara, Chairman IMA AMS for the guidance and leadership he has shown, Dr. Sanjeev Singh Yadav, Honorary Secretary IMA AMS for the freehand given for the preparation of Annals and reposing faith in my abilities.

I am grateful for the support received from all the office bearers of IMA AMS, words of encouragement from the Past Chairmen and Past Secretaries of IMA AMS, the cooperation and participation from all the State branches of IMA AMS.

My heartfelt thanks to Dr. Dilip Bhanushali for nurturing me in my IMA journey and Dr. Mohan Gupta for helping me learn the finer nuances of publishing the Annals.

I would like to place on record my sincere appreciation of Ms. Sarita, our office staff for the wonderful work rendered in coordinating with so many people to ensure timely publication of the Annals. Mr. Kantilal Shah and Mr. Murali from Atlas Printers deserve a special mention for transforming our academic efforts into such a beautifully designed publication.

My family has been a great source of strength throughout my tenure and I truly value their presence, support and understanding.

The greatest satisfaction for me, personally, would be if this publication saves patient lives though its readers.

Long Live IMA!

Dr. Srirang Abkari
Honorary Editor, Annals, IMA AMS



AMscON 2022

**Annual National Conference of
Indian Medical Association - Academy of Medical Specialities
And East Zonal Conference of IMA AMS**

Organized by
IMA BENGAL STATE BRANCH

**5th & 6th November, 2022
The Calcutta Boating & Hotel Resorts**

1 A/1J, East Topsia Road, JBS Haldane Avenue, Gobra, Kolkata, West Bengal 700046
(Adjacent to ITC Sonar Bangla and Science City)



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Ex MLA
State President,
IMA Bengal

Organizing Secretary
Dr. Santanu Sen, MP
Past National President
Honorary State Secretary,
IMA Bengal

Organizing Treasurer
Dr. Sourav Datta
Honorary Finance Secretary,
IMA Bengal

Conference Secretariat:
IMA Bengal State
Address of Correspondence: Dr. B C Roy IMA House
11/3, Dr. Bires Guha Street, Kolkata 700017
Contact No: +91 7003687488, +91 9903930575
Whatsapp @ 9674900957
Email: amscon2022@gmail.com



INDIAN MEDICAL ASSOCIATION (HQs.)



(Registered under the Societies Act XXI of 1860)

Mutually Affiliated with the British & Nepal Medical Associations

I.M.A. House, Indraprastha Marg, New Delhi-110 002

Telephones: +91-11-2337 0009 (10 lines), 23378680 / +91-9999116375, 9999116376, Fax: +91-11-23379470

Website: www.ima-india.org ; Email: hsg@ima-india.org



National President
Dr. Sahajanand Pd. Singh
+91-9334118698
np@ima-india.org

Immediate Past National President
Dr. J A Jayalal
+91-9443160026
lapsurgeon2001@yahoo.co.in

Honorary Secretary General
Dr. Jayesh M Lele
+91-9819812996
drjayeshlele@gmail.com

Honorary Finance Secretary
Dr. Anil Goyal
+91-9811101454
drgoyalhospital@gmail.com



21.10.2022
New Delhi

Message from National President, IMA

I am delighted to know that IMA Academy of Medical Specialities (AMS) is going to organise its Annual National Conference (IMA AMSCON 2022) on 5th & 6th November 2022 the conference will be organised by IMA Bengal State Branch under the Auspices of IMA AMS Head Office at The Calcutta Boating & Hotel Resorts, 1 A/1J, East Topsia Road, JBS Haldane Avenue, Gobra, Kolkata, West Bengal.

IMA Academy of Medical Specialities (AMS) is the one of the major wings of the Indian Medical Association (HQs.) The Annual National Conference (IMA AMSCON 2022) will enable our members to interact with each other and share their rich experiences of the medical practices.

I hope the scientific programmes of this conference will be great interest for our members.

I wish the organisers a great success.

Jai Hind Jai IMA

Sahajanand Prasad Singh

Dr. Sahajanand Prasad Singh

National President

Indian Medical Association (HQs.)

Priority in Rural Healthcare & Dignity of Profession

ग्रामीण स्वास्थ्य सेवा में प्राथमिकता एवं पेशे की गरिमा



Dr. Jayesh M. Lele

Hony. Secretary General
Indian Medical Association

Message

Greetings from Indian Medical Association!

It is a great pleasure to know that IMA Academy of Medical Specialties is releasing the prestigious Annual Annals for "MEDICAL EMERGENCIES" for the year 2022 during the IMA AMSCON 2022 the Annual National Conference of IMA AMS which is going to organize by IMA Bengal State Branch under the auspices of IMA AMS HQs on 5th & 6th November at Kolkata, West Bengal.

IMA AMS is doing a great job by releasing Annals and I hope it will provide useful material to its members. I am sure, this will enhance the knowledge and expertise of its members in the latest advancements in medicine and medical technology.

IMA AMS is the only platform where all specialists meet with each other and can deliberate on issues which are relevant in providing holistic treatment to patients by discussing interdisciplinary management for better outcome.

Such Conferences provide an opportunity for the members of the Indian Medical Association to have a democratic, healthy and meaningful interaction on issues pertaining to the medical profession and the health-related problems of the people of our country.

I convey my best wishes to the Advisory Board of Annals and I hope it would provide useful material to its members.

I wish the Annual Conference a tremendous success.

Long Live IMA!

Dr. Jayesh Lele

Honorary Secretary General, IMA



Dr. Vedprakash Mishra

Pro-Chancellor
Datta Meghe Institute of Higher
Education and Research
(Deemed to be University),

Message

It gives me immense pleasure and satisfaction to note that IMA Academy of Medical Specialities, IMA Bengal State Branch under the aegis of Indian Medical Association, National Headquarters, is organizing its Annual annals 'IMA AMSCON-2022' conference on 5th and 6th November, 2022 with a wide spectrum of academic activities pertaining to various specialities spread therein under its umbrella. The nature of discussion and deliberations envisaged are bound to be fruitful and productive, which would go a long way in generating appropriate strategies towards mitigation of the maladies at hand.

It is equally heartening to note that a commemorative souvenir is also been brought out on the great occasion which would be a genuine compendium for subsequent reference and follow-up by all concerned.

It is true that Covid times have unequivocally brought to the fore the role and relevance of medical doctors in the larger interest of men and mankind at the altar of making highest sacrifice at the cost of their lives. However, the material reality which stares in a very cognizable sense is worrisome for the profession as well as the medical fraternity on several counts including unabated violence against the Doctors and various policy frames which are and would continue to cause heavy prejudice beyond repairs.

It is imperative that a diligent stock of the scenario threatening in nature and scary in character needs to be taken note of and resisted with all might of collective strength so as to invoke an appropriate ambience for effective and meaningful rendering of the professional cause not for any selfish gains but to cater to the larger and highest interest of people and public at large.

Indian Medical Association as the unitary organization of medical professionals is the ray of hope, which in terms of its determined commitment to cater to the cause of profession and professionals is giving no stone unturned to invoke a healthy ambience in a cogent and credible manner. It is indeed a matter of great pride that the healthcare professionals have brought out their best face in the context of the grave scenario that has engulfed the entire world, which is exemplary by all cannons and yardsticks.

IMA Bengal State Branch with its great grand legacy is shouldering and partnering the entire responsibility of Indian Medical Association with great vigor and vitality blended in unfathomable commitment to cater to the larger cause.

My words realistically fall at bay to express my appreciation for the great and committed work that has been rendered by Bengal State IMA AMS and continues to render in an open ended manner which is exemplary in nature and emulative in character. The present annual conference that has been scheduled would definitely be availed by all concerned as a right forum for taking stock of the prevailing situation and also of the initiative that have espoused in the interest of profession and professionals and how with further strengthening the same can be carried out to its logical end.

I deem it my pleasure to extend my warmest wishes to the scheduled conference and to the members of the organizing committee for the notable initiative which would invariably turn out to be a landmark and a milestone on the annals of time.

Dr. Vedprakash Mishra



Dr. Prabhakara G.N.

Chairman
IMA AMS -2021-2022

Message

Greetings from IMAAMS Head Quarters.

I am very happy that we are releasing the Annals during AMSCON at Kolkata. I thank Our Dynamic Secretary and Hony Editor Dr Srirang Abkari for selecting a wonderful topic and is need of the hour.

A medical emergency is an acute injury or illness that poses an immediate risk to a person's life or long-term health, sometimes referred to as a situation risking "life or limb". These emergencies may require assistance from another, qualified person, as some of these emergencies, such as cardiovascular (heart), respiratory, and gastrointestinal cannot be dealt with by the victim themselves.^[1] Dependent on the severity of the emergency, and the quality of any treatment given, it may require the involvement of multiple levels of care, from first aiders through emergency medical technicians, paramedics, emergency physicians and anesthesiologists.

Any response to an emergency medical situation will depend strongly on the situation, the patient involved, and availability of resources to help them. It will also vary depending on whether the emergency occurs whilst in hospital under medical care, or outside medical care (for instance, in the street or alone at home).

Hope all these challenges will be clarified in this annals. I welcome all the members to attend National conference IMAAMS at Kolkata on November 5th and 6th. I thank all GC members, and the members who have cooperated with me. My special thanks to all the members who have contributed to Annals. Once again I thank Editor for bringing this issue.

Jai Hind - Jai IMA

Dr. G. N. Prabhakara

Chairman IMA AMS -2021-2022



Dr. E. Ravindra Reddy

National Vice President
Indian Medical Association

Message

It gives me immense pleasure to learn that Indian Medical Association Academy of Medical Specialties (IMA AMS) is organizing its Annual Conference on 5th and 6th November 2022 at Kolkata.

As an important academic wing of IMA, AMS is doing yeoman service to the medical fraternity. I would like to congratulate the entire team of IMA AMS for their sincere effort in carrying out its activities. I would like to place my special appreciation for the work done by Dr. Sanjeev Singh Yadav, the dynamic Hon. Secretary. He has been coordinating the activities of all its branches with great enthusiasm.

The eagerly awaited Annals of IMA AMS has been the hallmark publication of this wing. I am delighted to know that the theme for this year is Medical Emergencies. To have eminent clinicians contribute articles on this very important topic is indeed a blessing for the members to equip themselves in tackling emergencies and saving patient lives. Dr. Srirang Abkari, Hon. Editor, truly deserves a special mention for his untiring efforts in bringing out Annals of the highest academic standards. I would like to congratulate him for the wonderful academic work gone into making of the Annals.

My best wishes to the entire organizing team at Kolkata for the grand success of the conference.

Let IMA AMS scale new heights in academic excellence and become a hub of educational activities throughout the country.

Long Live IMA!

Dr. E. Ravindra Reddy
National Vice President
Indian Medical Association



Dr. Daggumati Sreehari Rao

Immediate Past Chairman,
IMA AMS (HQ)

Message

Dear Sir,

Warm greetings from TIRUPATI, Andhra Pradesh. Pray lord Venkateswara to bless us to serve the needy and poor.

First I would like to thank the office bearers of IMA AMS, IMA HQ, Speakers and Delegates, who attended IMA AMS NATCON 2021, It gives me immense pleasure to organised the IMA AMS NATCON 2021 under the auspices of IMA AMS HQ at the holy, mighty place and temple city of Tirupati on 19th and 20th December 2021.

Delighted to note that IMA AMS HQ Publishing the prestigious Annual Annals for "Medical Emergencies" for the year 2022.

I congratulate the Team IMA AMS HQ Lead by Dr. G. N. Prabhakara and Dynamic secretary Dr. Sanjeev Singh Yadav for continuing the incredible tradition of bringing out our IMA AMS Annals.

It is a great pleasure to know that IMA AMS NATCON 2022, will be organized by IMA AMS Bengal state on 5th and 6th November 2022 at Kolkata under the leader ship of IMA Past National president and organizing secretary AMS CON 2022- Dr. Santansen, M.P (RAJYA SABHA) DR. M.A.KASEM, organizing chairman,

I convey my sincere best wishes to the organizing team and I hope the delegates will have divine dharshan at sakthi sthall of Kalighat Kali temple, dedicated to the Hindu Goddess Kali, and also enjoy the hospitality with a feast of knowledge, awards and fellowships.

IMA AMS is the only platform where all specialists meet with each other and can deliberate on issues which are relevant in providing holistic treatment to patients by discussing interdisciplinary management for better outcome.

Academy of Medical Specialities has been flag bearer of keeping the doctors updated with recent developments in the field of medicine and surgery and it is the duty of the member doctors to keep spreading the message among non-members also that Academy is working for skill development and one has to take care of his or her skills to be updated regularly.

Wishing a very bright and grand successful event on this conference.

Dr. Daggumati Sreehari Rao

Immediate Past chairman, IMA AMS (HQ)



Dr. M.S. Ashraf

Past National chairman IMA AMS
Past National Vice President IMA Hq
Dr. BC. Roy National Awardee

Message

Dear Sir ,

Best Wishes

I am pleased to note that the annual Annals of Indian Medical Association – Academy of Medical Specialities (IMA AMS - 2022) will be released during the National Conference at Kolkata .

If you are prepared for an emergency theoretically and practically , the outcome would always be positive and successful . Hence the annals on this vital topic "Medical Emergencies" would enrich the knowledge and help us to meet the emergencies in the Triage with confidence .

I am confident that the annals will be useful to the members and practitioners alike .

I wish the National Conference Indian Medical Association - Academy of Medical Specialities (IMA AMS – 2022) all Success .

With warm regards ,

Dr.M.S.Ashraf

Past National chairman IMA AMS
Past National Vice President IMA Hq
Dr. BC. Roy National Awardee



Prof. Dr. A. Zameer Psha

President-IAGES (2017-18)

President, International College of Surgeons, India (2015-17)

Founder Chairman, Hospital Board of India - IMA, New Delhi

All India Chairman, IMA - AMS, New Delhi

Governor, Indian Region, ELSA (Endoscopic Laparoscopic Surgeons of Asia, Hongkong)

Chairman, Nursing Homes & Hospitals Board, Tamilnadu IMA State Branch

National Vice President, IAGES 2006 - 2008

State President, IMA, Tamil Nadu 2005-2006

Message

Dear Dr.Sanjeev Singh Yadav, IAM - AMS Greetings !

Delighted that IMA AMSCON - 2022 is being organized by IMA Bengal State under the Auspices of IMA AMS Head Quarters is being held on 5th & 6th Nov,2022 at Kolkdta.

IMA AMS the specialist academic wing of IMA is doing yeoman service to the multifarious specialities.

I wish you hearty Congratulations on this prestigious Annual Annals for "Medical Emergencies" for the year 2022.

Doubtlessly IMA is the mother of all specialities Associations. Am certain that you and your dynamic team will leave no stone unturned to make this academic bonanza a meteoric success.

I With Best Wishes and Regards,

Yours in IMA,

Prof. Dr. A. Zameer Pasha

Past Chairman, IMA - AMS (Hqrs)



Dr.Ajoy Kumar Singh

Ex.National VP IMA
Ex. Chairman IMA AMS

Message

Dear Dr Srirang Abkari

Greetings from Ranchi, Jharkhand.

It gives me immense pleasure in sending my greetings and best wishes for the Annals of IMA AMS, a publication by we doctors, for we doctors, a book sharing knowledge with each other. It is no new for IMA AMS, as long before it was there, but irregularly regular published, but new team has made it a regular publication so my heartfelt thanks, in 2022 IMA AMS Hqrs is publishing the prestigious Annual Annals for "MEDICAL EMERGENCIES" This Medical Emergencies Annals will be a boon and good Guide hand Book, to tackle the medical emergencies which becomes scary when handling such cases in I'll equipped hospitals and in remote health care outlets..

Every member of Academy will be benefited by it, thus we are justifying the need and purpose of this wing of IMA and justifying its need..

My best wishes to full IMA AMS present team who have given new heights to IMA AMS

My greetings and best wishes IMA AMS Hqrs publishing the prestigious Annual Annals ,this time on "MEDICAL EMERGENCIES" for the year 2022. Wishing Great success for IMA AMSCON 2022. at Kolkata on 5th and 6th November 2022

My best wishes to Dr. G. N. Prabhakara ,Dr.Sanjeev Kumar Yadav, and His dynamic IMA AMS team.

Yours truly,

Dr. Ajoy Kumar Singh

Ex.National VP IMA
Ex. Chairman IMA AMS



Dr. M. Bhaskaran

Past National Chairman
IMA AMS H. Qrs

Message

Dear Dr. Sanjeev Singh Yadav,

I am extremely happy to understand that IMA AMS is publishing an "Annual ANNALS for Medical Emergencies " along with the Annual Conference of IMA AMS 2022.

IMA AMS is the Speciality Academic wing of IMA, which includes all Speciality wings and coordinates all speciality associations.

Our Medical Profession is developing very fast with newer methods of diagnostic procedures, newer modalities of management of diseases & medical emergencies and newer molecules of drugs. So it is absolutely necessary for the practising specialists to update the latest knowledge for the better management of Diseases and Emergencies. IMA AMS is conducting a number of Continuing Medical Education Programmes including Treatment Protocols in different Specialities for the practicing Doctors, which in turn will be benefitted by the Society.

I am happy to note that IMA AMS under the Leadership of Dr. G .N. Prabhakara as Chairman and Dr. Sanjeev Singh Yadav as Secretary with other Office Bearers have done exemplary activities in the last one year , even when the Covid Pandemic is still prevalent in the Society .

I am sure the Scientific feast will enlighten our members and will be cherished forever. All CONGRATULATIONS and BEST WISHES for the CONFERENCE

Dr. M. Bhaskaran

Past Chairman, IMA AMS



Dr. Madhuchanda Kar

Past National Chairman
IMA AMS H. Qrs

Message

Dear members and colleagues,

I hereby congratulate IMA AMS H. Qrs for the noble initiative of publishing the prestigious Annual Annals on "MEDICAL EMERGENCIES" for the year 2022. I wish you all success for its release during IMA -AMSCON 2022.

Medical Emergencies are perhaps the most common clinical situations that are faced by the practitioners, faculties and administrative leaders of all fraternities of medical science. It is very pertinent that all of us have maximum knowledge-base in this regard. In this context IMA Academy of Medical Specialities can really show the way forward. Congratulations to IMA-AMS H.Qrs for this pro-active and extremely relevant effort to explore such important Medical Emergencies. I thank all those who have contributed to this Annals on "MEDICAL EMERGENCIES"

Your's Sincerely,

Dr. Madhuchanda Kar

Past National Chairman IMA AMS H. Qrs



Dr. M. S. Hari Babu

Past National Secretary
IMA AMS

Message

Dear Sir ,

Best Wishes

I am delighted that IMA AMSCON-2022 is being organized by IMA AMS at Kolkata on 5th & 6th November 2022. IMA AMS the speciality wing of IMA is doing yeoman service to all different specialities.

Without doubt IMA AMS is mother of all specialities Association.

I sincerely congratulations to the organizers of IMA AMSCON-2022 for the grand success of the conference.

I am very sure that the conference will be a scientific feast which enlighten our members.

With warm regards ,

Dr. M. S. Hari Babu

Past National Secretary IMA AMS



Dr. E. Prabhavathi

Consultant Gynec Laparoscopic Surgeon
Past National Secretary & Editor
IMA AMS Hqrs

Message

As the past National Secretary of Academy of Medical specialties, I take immense pleasure in giving this message for Annals of IMA AMS in the forthcoming IMA AMSCON 2022 Nov 5th and 6th 2022 at Kolkata.

The Annals of IMA AMS has always been pioneer in updating medical fraternity with latest scientific content and advanced treatment protocols. As the current post Pandemic period has been emerging with many newer and diversified clinical presentations, they pose greater challenge to the treating clinicians. This year, the Annals highlights CURRENT MEDICAL EMERGENCIES and their updates. With great confidence in pursuit of excellence, this annals is going to provide expertise knowledge to the members which guides better patient care.

I congratulate the advisory board and editorial board of the annals for publishing this journal with great efforts.

Dr. E. Prabhavathi

Consultant Gynec Laparoscopic Surgeon
Past National Secretary & Editor
IMA AMS Hqrs



From Secretary's Desk



Dr. Sanjeev Singh Yadav

National Secretary IMA AMS
Hony. Secretary, IMA AMS Hqrs

I am really honored as Secretary IMA AMS to communicate with you through these Annals. IMA Academy of Medical Specialities was established in the year 1979 with the following objectives:

- To provide a forum to Specialists and Super-specialties of all branches of Medicine to discuss multi-disciplinary matters of academic interest
- To promote and encourage unity among the members of IMA
- To enhance image of IMA
- To increase Life Membership and Fellowship of IMA AMS
- To update all the members of IMA of the recent advances in the field of Medicine and allied subjects
- To conduct C.M.Es all over India
- To conduct various Specialty and sub-specialty courses

I am pleased to send this message through the Annals of IMA AMS, bought out for the convenience of the IMA Doctors. The Annals will provide a gist of the prevailing diseases for the benefit of better treatment to the patients and a comprehensive approach by the treating physicians.

Still a long way to go, the need to publish Annals every quarterly, must be the goal of this Academic Body. Being busy Doctors it has been difficult to get the Articles in time. I request all the Specialists to come forward and send the articles as soon as possible for publishing the same and making the AMS Annals a regular affair.

I would like to congratulate our Editor (Annals) Dr. Srirang Abkari for his tirelessly day and night effort, to bringing out **COVID-19, EPILEPSY and now, MEDICAL EMERGENCIES** Annals. Dr. Srirang Abkari will be taking charge as Hony. National Secretary of IMA AMS Hqrs along with Dr. Pankaj Mutneja, National Chairman Elect-2022-2023 IMA AMS Hqrs, Dr. Nomeeta Shiv Gupta, National Chairman Elect-2023-2024 IMA AMS Hqrs and Dr. Nibedita Pani, Vice Chairman Elect 2022-2024 IMA AMS Hqrs in December at Allahabad IMA National Conference.

AMS Statistics:

19	State Chapters	195	Branch Chapters
16401	Life Members	2545	Fellows as on the date

Life Memberships & Fellowships received from 1st Jan 2022 to till date

Life Memberships - 437 Fellowships - 39

Uttar Pradesh State Chapter has opened "**Jhansi**" New Local Branch Chapter. Branch Chapter Inaugurated by Dr. Surya Kant, National Vice Chairman IMA AMS Hqrs

The main Activities of IMA AMS during this financial year are as under.



1. **On 2nd April 2022**, as per the directions of IMA Hqrs, National IMA AMS Office Bearers are participated in "**IMA PROTEST DAY**". Justice for Dr. Archana Sharma.
2. **On 9th April 2022**, Dr. Sanjeev Singh Yadav, AMS and National IMA Senior Leaders are participated on "Ethical Issues faced by Medical Profession" organizing by IMA Hqrs on virtual way.
3. **On 16th April 2022**, submitted IMA AMS Activity Report on the occasion of Central Working Committee Meeting on 16th & 17th April 2022 at Chandigarh.
4. **On 22nd May 2022**, IMA National President Dr. Sahajanand Prasad Singh visited IMA AMS Head Office Hyderabad. All IMA & AMS Office Bearers are participated and Honored to National President.
5. **On 28th May 2022**, 36th Governing Council Meeting & IMA AMS National Regional Meeting held on 28th May 2022, at Hubli, Karnataka State, the meeting was presided over by Dr. G. N. Prabhakara National Chairman IMA AMS, Dr. Sahajanand Prasad Singh, National President IMA HQs, Dr. J. A. Jayalal, Imm. Past National President IMA HQs, Dr. Ravi Wankhedkar, Past National President, IMA HQs, Dr. E. Ravindra Reddy, National Vice President IMA HQs, Dr. J. A. Jayalal, Hony. Secretary General IMA HQs, Dr. Sanjeev Singh Yadav, Hony. Secretary IMA AMS Hqrs, Dr. B. N. Reddy, Joint Secretary, IMA AMS Hqrs, Dr. Kateel Suresh Kudwa, President IMA Karnataka, Dr. Ramalingappa Antarthani, Director KIMS Hubli, Dr. S. M. Prasad, Secretary IMA Karnataka, Dr. S. B. Lakkol, President Elect IMA Karnataka, Dr. S. Y. Mulkipatil, President, IMA Hubli, Dr. Ishwar Hosmani, Chairman IMA Annual CME-2022 and Dr. M. Sampath Rao, President IMA Telangana State and Other Governing Council members of IMA AMS from all over India are attended this meeting. The main agenda of conducting of meeting is how to improve our Membership, Courses of IMA AMS, Regional and Zonal Conferences of North, South, East, West and central hosting by IMA AMS, AMSCON-2022, and Fellowships of IMA AMS.
6. **On 1st July 2022**, IMA AMS Hqrs under the IMA Hqrs Conducted for **BLOOD DONATION CAMP** is associated with Abbott India Pvt Ltd at Abbott Office in Hyderabad. Dr. Jayesh Lele, Hony. Secretary IMA Hqrs initiative for the camp is appreciative and he has been doing it for the past few years. Shri Ajay Mishra, Chairman Red Cross Society inaugurated the camp on 1st July 2022 at 10:30 AM. Mrs. Mauha M from Abbott, Dr. Sanjeev Singh Yadav, Hony. Secretary AMS Hqrs, Dr. B. Narendra Reddy, Joint Secretary IMA AMS Hqrs, Dr. Gattu Srinivasulu, Finance Secretary IMA TS and other AMS Office Bearers Staff of AMS, Abbott and Red Cross Society are present. 52 donors participated in this camp.
7. **On 15th August 2022**, Dr. Sanjeev Singh Yadav, Hony. Secretary AMS Hqrs participated Independent Bharath 75 yrs of Mahotsav on 15th August 2022, at IMA Building, Hyderabad along with IMA Hyderabad City Branch and IMA Telangana State.
8. **On 17th Sept to 24th Sept 2022**, National **IMA AMS South Zone Conference-(AMSSZCON-2022)** (Hybrid Meeting) Inauguration held on 17th September 2022, AMSSZCON 2022- Indian Medical Association academy of medical specialised National AMS South zone conference 2022 was conducted by IMA Cuddalore Branch, Tamil Nadu State from 17/9/2022 to 24/9/2022. National Leaders and State Leaders are participated. The **inaugural function** was conducted from 3pm to 4pm 3pm, National and State IMA Leaders participated in the program.
9. **On 16th September 2022**, ASGE (The American Society for Gastrointestinal Endoscopy) conducted **Gastro Power Summit 2022** associated with IMA AMS Hqrs on 16th September 2022 on virtual way. Dr. Jayesh Lele, Hony. General Secretary IMA Hqrs, Dr. Suryakant, Vice Chairman IMA AMS Hqrs, Dr. Sanjeev Singh Yadav, Hony. Secretary IMA AMS Hqrs participated on behalf AMS Hqrs.
10. **On 9th October 2022**, HYBIZ TV HEALTH CARE AWARDS at HICC Novotel. Dr. Sanjeev Singh Yadav, Hony. Secretary IMA AMS Hqrs being felicitated and received Award from our Minister of Medical & Health , Govt. of Telangana Shri T. Harish Rao. It is well appreciated by our former



Annual Journal of National AMSCON - 2022

Indian Cricket Captain Kapil Dev.

11. IMA AMS Kerala, Tamil Nadu, Karnataka, Maharashtra, Assam, Orissa, Bengal, Andhra Pradesh & Telangana States are conducted webinars with Associate of Various Specialties under the IMA AMS Hqrs. Dr. G.N. Prabhakara, Chairman and Dr. Sanjeev Singh Yadav, Hon. Secretary IMA AMS Hqrs and various State Chairman & Secretaries and IMA senior leaders are participated all webinars.

Suggestions & Appeal:

1. Request to form a new IMA AMS State Chapter to the following States, few IMA States have not yet formed into the IMA AMS State Chapters, i.e. **ARUNACHAL PRADESH, CHANDIGARH, GOA, HIMACHAL PRADESH, MANIPUR, MEGHALAYA, MIZORAM, NAGALAND, SIKKIM, JAMMU & KASHMIR, PONDICHERRY and TRIPURA.**
2. A State Chapter shall be established in each State, if there are 100 or more Life Members of the Academy in that State.
3. Request to State Presidents and Hon State Secretaries and to the Chairmen and State Secretaries of IMA AMS to increase membership and fellowships of IMA AMS.
4. State Chapters/Branch Chapters to conduct at least one activity in every month either CME or Webinar on behalf of IMA AMS in your respective State Chapters and their Branch Chapters involving basics Speciality. If you can conduct more than 3 to 4 webinars in a month. **We IMA AMS Hqrs providing free Zoom Link to conduct State/Branch webinars via IMA AMS Hqrs.** AMS State Chapter and National Chapter must be included in that programme. The IMA AMS Hqrs will recognize your services which will result in recognition of your efforts and you will be eligible for AMS National Awards in the National Conference (AMSCON) of IMA AMS.
5. As per the above membership list, if any branch membership is exceeding minimum 10 members, your branch is eligible for Share of LMS fee. So that increases membership to enroll all qualified doctors in IMA AMS.
6. And also we request to enroll Membership & Fellowships at least three as members of IMA AMS to strengthen our AMS which is working towards reaching new goals and Academic heights in the coming years. And also to encourage conducting Speciality Courses in your respective States.

My sincere thanks to our Chief Patron Dr. Ketan Desai, Dr. Sahajanand Prasad Singh, National President IMA Hqrs, Dr. J. A. Jayalal, Imm. Past National President, IMA Hqrs, Dr. Jayesh M Lele, Hon. Secretary General, IMA Hqrs, Dr. Anil Goyal, Finance Secretary IMA Hqrs, Dr. G. N. Prabhakara, National Chairman IMA AMS Hqrs, Dr. Suryakant, Vice Chairman, IMA AMS Hqrs, Dr. D. Sree Hari Rao, Imm. Past Chairman IMA AMS Hqrs for their valuable guidance and suggestions.

My Personal thanks to Dr. E. Ravindra Reddy, Vice-President IMA Hqrs 2021-2022 (from Telagnana) for constant guidance and also to the other Members of IMA National Body.

My sincere thanks to the Continues Guidance by Senior IMA luminaries in conducting the day to day affairs of AMS is always a gratitude and well wishes by our senior leaders, Dr. Vinay Agarwal, Dr. S. Arulrahj , Dr. G. Samaram, Dr. Vedprakash Mishra, Dr. Marthanda Pillai, Dr. K. Vijay Kumar, Dr. Ravi Wankhedkar, Dr. Shantanu Sen, Dr. Rajan Sharma, Dr. R. V. Asokan and all other senior IMA members And also thanks to, Joint Secretaries of IMA AMS Hqrs and Office Staff of IMA AMS Hqrs.

My Hearty wishes to Dr. Sharad Kumar Aggarwal, National President Elect-2022-2023, Dr. R.V. Asokan, National President Elect-2023-2024, Dr. Anilkumar J Nayak, Elect Hon. Secretary General Elect 2022-2024, IMA Hqrs and Dr. Shitij Bali, Finance Secretary Elect 2022-2024, IMA Hqrs.

Long Live IMA & IMA AMS

Dr. Sanjeev Singh Yadav

National Chairpersons



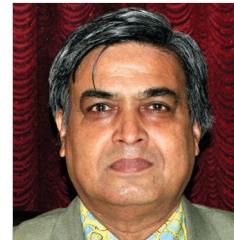
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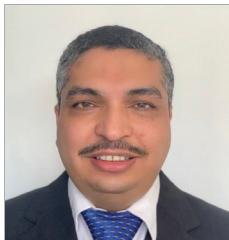
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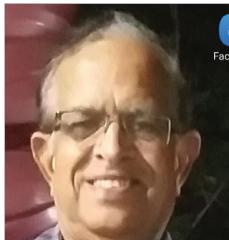
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*Articles
on
Medical Emergencies*



Sepsis and Septic Shock

Dr. Sudha Vidyasagar
HOD Medicine, VHS, Chennai

SEPSIS AND SEPTIC SHOCK

Infectious diseases form a major cause of mortality and morbidity in all developing countries. Cutting across specialties, infections can occur in any organ system and cause life threatening illness. However infections themselves may not cause all complications. Mortality in many infections is due to the occurrence of **sepsis**, which is the host response to infections..

SEPSIS

What is sepsis ?Sepsis is the dysregulated immune response to the presence of an infection. This dysregulated immune response results in organ dysfunction. Major organs such as the liver, kidney, respiratory system , heart and central nervous system are involved in the damage caused by sepsis. Thus in recent times there has been a shift of focus from just the bacteria and the infection to the host response. In fact it is this response resulting in life threatening organ dysfunction , which may be collateral damage, that decides ultimate prognosis. The sequential organ failure assessment (SOFA) score is used to decide prognosis in sepsis.

The most dangerous complication of sepsis is septic shock. It is defined as fall in blood pressure with a mean arterial pressure of less than 65 millimetres of Hg, despite adequate fluid therapy. Vasopressors are needed to maintain blood pressure adequate for organ dysfunction. Hypotension, in turn causes increased lactate levels more than 18 milligrams per dl. Thus, the definition of septic shock incorporates these two criteria of low BP and high lactate. Recognition of septic shock is very important as it has a high

mortality of 30 to 40% even in the best of centres. The good news however is that early recognition and intervention saves lives.

Pathophysiology.

Septic shock is defined as sepsis that has circulatory cellular and metabolic abnormalities.

In response to infection, the host releases cytokines which are inflammatory molecules involved in fighting the infection. These are IL6, tumour necrosis factor alpha, and various other cytokines. This activation of the immune system is associated with organ dysfunction resulting in liver and kidney damage , acute respiratory distress syndrome, CNS depression, and thrombocytopenia. There is also severe myocardial depression. Further, there is tremendous vasodilatation and endothelial dysfunction leading to under filling of the vascular system. The depressed myocardium and the dilated vascular bed together combine to cause profound hypotension. Thus the patient with sepsis has decreased main arterial pressure, which is called septic shock.

Criteria for septic shock

1. MAP< 65mm of hg despite fluid resuscitation,requiring inotropes
2. Lactate > 18mg/dl
3. Evidence of sepsis and exclusion of other causes of shock.

This criteria maybe somewhat modified for patients with hypertension as their baseline systolic blood pressure may be higher. A decrease in systolic pressure more than 40 mm from

baseline or a MAP<80 mm maybe considered as shock in these patients..

Source of sepsis

The commonest source of sepsis is the lung and respiratory infections caused by gram positive and gram negative organisms cause grave sepsis, in susceptible individuals .. Abdominal infections such as cholecystitis, necrotising pancreatitis, are the next common cause. Bloodstream and urinary infections follow. Emphysematous pyelonephritis is common in diabetes and may need drainage through a DJ stents or percutaneous nephrostomy

Investigations in sepsis

It is important to have a checklist of investigations to be sent initially in any patient with sepsis . Basically these investigations aim at finding out the source of sepsis, degree of multi organ dysfunction.

The list is as follows:

1. Cultures from blood and appropriate body fluids such as urine, sputum and stool should be sent.
2. Liver and renal function tests, a complete blood picture and peripheral smear. Serum lactate for tissue perfusion adequacy.
3. Chest X-ray ,ABG and Echocardiogram, for assessing respiratory and cardiac function.
4. Imaging such as ultrasound abdomen and CT scan of thorax and abdomen,or MRI abdomen , as and when necessary.
5. Bio markers such as procalcitonin and CRP can be repeated for assessing improvement

Management of septic shock

Sepsis is a medical emergency associated with significant mortality the investigations and the management of the condition have to be simultaneous. The management hinges on three basic principles. The first priority is to maintain mean arterial pressure and save tissue perfusion and hence limit organ dysfunction. The second

and probably the most important measure is identifying and treating the infection that caused the septic shock effectively. The third aspect of management is supportive care while waiting for the antibiotics to act.

Fluid resuscitation :

The profound vasodilatation of septic shock leading to hypotension is first corrected by administration of fluids. Before administration of fluids routine investigations like complete blood picture renal and liver function test and electrolytes including lactate levels, are sent to the lab.

The fluid resuscitation has to be fast and furious. It is recommended at patients should receive 30 ml per kg of fluid as bolus over the first three hours. Fluid boluses of 500 ml each are used. Normal saline or ringer's lactate is recommended as the fluid of choice. This is called fluid challenge. At the end of this challenge it is expected that the patient will improve his blood pressure to maintain MAP of more than 65 mm of hg. There have been debates as to which type of fluid is best for shock. Crystallite such as normal saline score over colloids such as albumin in several studies such as the SAFE study. Hence the current recommendation is for crystalloids only.

There has been controversy regarding how to measure fluid responsiveness. When do we know that we have given adequate fluid? The BP alone is not an accurate measure of filling up the vascular compartment.

One of the simple bedside techniques of finding out if fluid resuscitation is adequate is by looking at IVC collapsibility. If the IVC is still collapsible and not full there maybe a need for more fluid. However this technique has poor sensitivity and specificity and significant observer variation. More sophisticated techniques such as passive leg raising to increase venous return with simultaneous measurement of stroke volume by echo has been tried. But none of these is accurate or satisfactory.

A simple clinically useful measure is to calculate the hourly urine output. If the patient puts out

enough urine (0.5ml/kg/hr) then probably the vascular compartment is adequately filled. Further one of the most important and dangerous complications of septic shock is acute kidney injury. This must be prevented at all costs. The urine output is a reassuring parameter assessing ongoing adequate kidney function.

Dangers of fluid management

All guidelines about fluid management must be tempered with sound clinical sense. Especially in the elderly the recommended volume of fluid maybe dangerous as the patient may have poor cardiac function, and excess fluid may lead to pulmonary edema. Hence it is important to individualise fluid management. Further, clinical ongoing judgement is a must to decide and very the amount of fluid given.

Several patients which septic shock also have acute respiratory distress syndrome(ARDS). They are breathless and they may need ventilatory support. This group of patients also require lesser amounts of fluid to be given as excess fluid may worsen ARDS.

Stage of septic shock

However in patients do not improve their blood pressure with fluids the need for inotropes arises. This is the stage of septic shock.

At the stage it is best to place a central line to deliver Inotropes as there efficacy is best when delivered centrally.

Which inotrope should be chosen?

There are three inotropes to choose from: nor adrenaline, adrenaline and vasopressin. Nor adrenaline is the first inotrope of choice. It acts by causing vasoconstriction of the vessels without causing tachycardia. If BP is not maintained by this, adrenaline can be used. It is a cardiac inotrope and helps the heart to pump better. One of the limiting side effects of adrenaline is tachycardia.

The third inotrope that can be used is vasopressin which again acts on the vascular smooth muscle. These drugs are added sequentially to maintain MAP at acceptable levels. However they are all limited by their tendency to cause unacceptable tachycardia or profound vasoconstriction leading to gangrene of the digits.

Dobutamine is used for myocardial dysfunction which is common in sepsis. However it will not increase BP and hence cannot be depended upon to maintain MAP.

It is important to note that inotropes can be used along with fluids, if blood pressure does not come up. The assessment or the need of massive pressures and fluids must be ongoing throughout the treatment septic shock.

Table 2.3 Summary of commonly used vasopressors

	Dose	Receptor	Major effect
Norepinephrine	0.01–3 mcg/kg/min	$\alpha >> \beta$	Vasoconstriction
Epinephrine	0.01–0.7 mcg/kg/min	$\alpha & \beta$ non-selective	Vasoconstriction <i>Note:</i> At higher doses Decreased splanchnic blood flow, hyperglycemia, hyperlactatemia, tachyarrhythmias
Dopamine	2–20 mcg/kg/min Predominant α and β action is seen at doses >10 mcg/kg/min	$DA > \beta > \alpha$	Vasoconstriction <i>Note:</i> Can cause tachyarrhythmias at doses >10 mcg/kg/min
Vasopressin	0.03 U/min (addition as a norepinephrine sparing)	V1	Vasoconstriction <i>Note:</i> While discontinuing, it should be slowly tapered

Steroids in septic shock

The role of steroids in septic shock is controversial. Steroids are known to increase the sensitivity of the vascular system to inotropes. Further there may be a relative steroid deficiency in sepsis. However they are double edged swords as they can increase inflammation and organ failure. Also they may cause unacceptable high sugars. Several trials have addressed this question. Currently the surviving sepsis guidelines gives a role for steroids. These can be used when the BP is still low, with inotropes. Hydrocortisone is the recommended steroid, in a dose of 50 mg iv 6-8 th hourly.

Antibiotics in sepsis

Since sepsis is secondary to an infection early usage of antibiotics is the single most important factor which changes prognosis. Studies have shown that for every 1 hour delay in the use of antibiotics the mortality in sepsis increases by 6 to 7%. Further the mortality in septic shock decreases by 50%, if the right antibiotic is given within the first 6 hours !

The organisms causing sepsis vary from hospital to hospital, and it is good to have an idea of the type of organisms encountered in every ICU. Common organisms are MRSA and E.coli. Of late multi drug resistant klebsiella, and Acinetobacter are becoming more common, as are enterococcus species.

Antibiotics are best delivered after drawing appropriate cultures such as blood, urine, sputum or pus. However , delay in drawing cultures should not delay the delivery of antibiotics.

Choice of antibiotics in septic shock has to be based on an intelligent guess work as to the source of infection. Patient's profile in terms of age, commodities and history usually give a clue to the site and source of infection. Antibiotic are thus chosen based on the clinician's judgement of the likely infection and hence must be empirical and broad based initially.

Most clinicians would begin with either 3rd generation cephalosporins like ceftriaxone, cefoperazone sulbactam, or a semi synthetic penicillin like piperacillin tazobactam. For E.coli bacteremia, meropenem maybe the drug of choice.

Table 2.2 Risk factors for select organisms^a

MDR GNB	MRSA	VRE	Candida
<ul style="list-style-type: none"> IV antibiotics within 90 days Five or more days of hospitalization prior to onset Requiring acute renal replacement therapy Septic shock Colonization with MDROs 	<ul style="list-style-type: none"> Colonization with MDROs Recent MRSA infection Known MRSA colonization Purulence or abscess of the skin or IV access site Severe rapidly progressive necrotizing pneumonia 	<ul style="list-style-type: none"> Liver transplant Known colonization Prolonged use of broad-spectrum antibiotics Profound immunosuppression 	<ul style="list-style-type: none"> Central venous catheter Broad-spectrum antibiotics Plus, one of the following <ul style="list-style-type: none"> – Parenteral nutrition – Dialysis – Recent abdominal surgery – Necrotizing pancreatitis – Immunosuppressive agents

^aAdapted from Derensinski and Stan. "Severe Sepsis and Septic Shock Antibiotic Guide". Stanford Antimicrobial Safety and Sustainability Program. Stanford Health. May 2017

ORGANISM	ANTIBIOTIC IV
Gram negative sepsis	Piperacillin-tazobactum Meropenem cefaoperazone+sulbactam/Cefepime Polymixin/ colistin Tigecycline /minocycline
Gram positive: staph streptococcus	Vancomycin/teicoplanin Ceftriaxone+azithromycin
For pseudomonas	Anti pseudomonal drug +aminoglycoside,if bacteremia is suspected
For neutropenic sepsis Line related /prior antibiotic Tt Aerobic –intra abdominal	Above +antifungal Metronidazole

It is important to note that 30-40% of cultures may be negative, especially if there has been prior antibiotic exposure . However the prognosis does not change with the positivity of the blood cultures

Antibiotics must be given intravenously. Some of these need to be given a loading dose and several of them need to be infused over 2 to 3 hours for adequate efficacy. Narrowing down of the antibiotics to more specific ones is done with evidence of site of infection from chest X-ray ,ultrasound, or can be based on appropriate blood cultures or tissue cultures.

The de escalation of antibiotics is based on clinical improvement and appropriate investigations. Generally treatment is for 7-10 days .

The table below, gives the timelines and goals of treating sepsis :

Surviving sepsis campaign bundle (2018)is given below :

Source control

They are infections where surgical intervention may be needed to control the source of infection. One such example is necrotizing fasciitis where the surgeon's role for debridement is more important than just giving antibiotics. Abscesses in the liver or subcutaneous tissue must be drained or

Panel 2: Surviving Sepsis Campaign hour-1 bundle (2018 update)¹⁴

- "Measure lactate level. Re-measure if initial lactate is >2 mmol/L" (weak recommendation, low quality of evidence)
- "Obtain blood cultures prior to administration of antibiotics" (best practice statement)
- "Administer broad-spectrum antibiotics" (strong recommendation, moderate quality of evidence)
- "Rapidly administer 30 mL/kg crystalloid for hypotension or lactate ≥4 mmol/L" (strong recommendation, low quality of evidence)
- "Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg" (strong recommendation, moderate quality of evidence)

MAP=mean arterial pressure.

eliminating sepsis. Pyelonephritis with blocked urinary tract needs stenting to drainage with DJ stenting ,or percutaneous nephrostomy is needed for renal abscess. An empyema must be drained by an intercostal tube ,to prevent bacteraemia and septic shock. Non-removal of source will lead to partial treatment of sepsis or recurrence of infection.

Biomarkers in sepsis :

Role of procalcitonin:

Procalcitonin is a bio marker that is increased in bacterial infections. It rises within 6 hours of the onset of the infection and falls rapidly within 24

hours with control of infection. Procalcitonin in value of more than 0.05 milligrams per decilitre is suggestive of bacterial sepsis. The levels of procalcitonin may not correlate with the degree of infection. However it is very useful as a bio marker or assessing follow up of control of infection. Antibiotics can be deescalated based on falling procalcitonin levels to 50% or near normal levels in addition to clinical improvement.

CRP is another common biomarker that is used to diagnose and monitor infection. However, it can be raised even in inflammatory arthritis like rheumatoid arthritis. Further CRP rises slowly after 48 hours, and falls slowly, and cannot be used to deescalate antibiotics.

Supportive care

Patients with septic shock are invariably prone to multi organ dysfunction. A significant percentage may have ARDS requiring ventilatory support. Those who have acute kidney injury with serious metabolic acidosis, hyperkalemia, or anuria may require dialysis. Those who have hypotension may not tolerate regular dialysis and need continuous renal replacement therapy.

Bicarbonate infusions may be needed for pH less than 7.1, to tide over the crisis. Hypoglycaemia is common in sepsis due to multi organ dysfunction and inflammatory cytokines causing low sugar. This should be watched for and treated urgently. Sepsis can also cause stress hyperglycaemia, which should be tackled by insulin infusions. It is best to maintain blood sugar between 140-180mg/dl in any critically ill patient.

Blood transfusion may be needed in those with haemoglobin less than 7 grams per decilitre. Platelet counts may fall to dangerous levels, and some patients may need platelet transfusions, especially if less than 10,000 cells/mm. In patients with liver failure fresh frozen plasma is given to correct abnormal prothrombin time.

All patients with septic shock may be bed ridden in the ICU, and may need thromboprophylaxis, for prevention of deep vein thrombosis. This can be done by mechanical stockings, or by heparin

injections. Because they are prone to develop stress ulcers, PPIs may be needed during their critical illness.

Feeding and maintaining of caloric intake and protein is important in the ICU to prevent malnourishment. This is best done by enteral feeding. Some patients may need total parenteral nutrition, if their cause of sepsis is intraabdominal, and feeding is delayed or difficult. Any fever in the ICU may increase tachycardia and cause worsening of cardiac and brain function. Hence it should be aggressively treated with anti-pyretics, and cooling.

The ICU check list of FASTHUGS BID

- Feeding/fluids
- Analgesia
- Sedation
- Thromboprophylaxis
- Head up position
- Ulcer prophylaxis
- Glycemic control
- Spontaneous breathing trial
- Bowel care
- Indwelling catheter removal
- De-escalation of antibiotics

Goals in management:

The following are the goals in management of sepsis ,and adherence to this timelines and guidelines, will help patients recover from life threatening septic shock.

Changes in management of sepsis and septic shock:

The changes in management are that the MAP of hypertensives may need higher targets. The surviving sepsis campaign now recommends, that the management of each patient is different, and hence , fluids and inotropes and antibiotics, should be personalised, rather than protocolised. The value of dynamic hourly monitoring of BP and urine output and fluid status is important to make necessary changes , along the course of management to propel patient to recovery,.



Box 2.3 Goals in the Management of Sepsis

Goals in the management of sepsis:

- MAP \geq 65mm Hg
- Lactate < 2mmol/L
- P/F ratio >200
- SpO₂ 88–92%
- Urine output > .5ml/kg/h
- Hemoglobin > 7g/dl
- Blood glucose < 180mg/dl
- No dyselectrolytemia
- No acid base disbalance

Other measures:

- Place a central venous catheter
- Peptic ulcer prophylaxis
- Venous thrombosis prophylaxis
- Nutritional support
- Pain management
- Sedation vacation

The role of the immune system in sepsis is still ununderstood. Hence the role of immunomodulators to down regulate the immune system, has not been defined correctly, and is still experimental.

Lastly, precision medicine is here to stay. We know that the response of each host to infection is vastly varied ,and hence the occurrence of septic shock is also unpredictable , in terms, of which patient is at risk. Future studies may help to define this more clearly, and management may become more accurate and focussed, according to host response.



Status epilepticus

Dr Ketaki Pradeep Patwardhan

Consultant Neurologist, Neuro One Brain and Spine Center
Vantmure Corner, Miraj, Maharashtra, India;
drketakipatwardhan@gmail.com

1) Introduction

Status epilepticus (SE) is a relatively common medical and neurologic emergency that requires prompt evaluation and treatment. Historically, the International League Against Epilepsy (ILAE) and others defined status epilepticus as a single epileptic seizure of >30 minutes duration or a series of epileptic seizures during which function is not regained between seizures in a 30-minute period. However, the society of Neurocritical care revised the definition to any seizure lasting more than 5 minutes¹.

A significant proportion of both children (16 to 38%) and adults (42 to 50%) with status epilepticus have a history of epilepsy. The short-term mortality (within 30 days) of status epilepticus ranges from 7.6 to 22% across all age groups and is highest amongst the elderly¹. Hence it is imperative for medical practitioners to be aware about this neuro-emergency.

2) Definition

Generalized convulsive SE in adults and children older than 5 years was operationally defined as "...e"5 min of (1) continuous seizure or (2) two or more discrete seizures between which there is incomplete recovery of consciousness².

The **proposed new definition of SE** is as follows:

This definition is conceptual, with two *operational dimensions*:

The first is the length of the seizure and the **time point (t_1)** at which the seizure should be regarded as an "abnormally prolonged seizure."

The second time point (t_2) is the **time of ongoing seizure activity** beyond which there is a risk of long-term consequences.

Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected². It is ideal that patient should receive treatment during the

Type of SE	Operational dimension 1 Time (t_1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t_2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic-clonic SE	5 min	30 min
Focal SE with impaired consciousness	10 min	>60 min
Absence status epilepticus	10–15 min	Unknown

shortest time dimension i.e.t1. The time dimensions for generalized and focal seizures are different.

Classification of SE as per axes^{3,4}

The purpose of the diagnostic axes is to provide a framework for clinical diagnosis, investigations, and therapeutic approach for each patient⁴

Previously, in 1970, the axes encompassed (1) clinical seizure type (2) electroencephalographic ictal and interictal expression (3) anatomic substrate(4) etiology, and (5) age. In the 1981 revision, the axes were limited to the seizure type and EEG expression (ictal and interictal) (Classification 1981)⁴.

At least half of the patients with SE do not have epilepsy or specific epilepsy syndromes, they have SE due to acute or remote central nervous system or systemic illness. Therefore, the axes used previously needed to be modified.

Ideally, every patient should be categorized according to each of the four axes-semiology, etiology, age and EEG.

At initial presentation, the approximate age of the patient and the semiology will be immediately assessable. The etiology will be apparent less frequently and may take time to identify. It is also recognized that EEG recordings will not be available in many settings, particularly at presentation.

However, the EEG will affect choice and aggressiveness of treatment, prognosis, and clinical approaches, so an EEG should be sought soon. Also some forms are reliably diagnosed on EEG only⁵.

1. Semiology – Type of seizure

This axis refers to the clinical presentation of SE and is therefore the mainstay of this classification. The two main taxonomic criteria are:

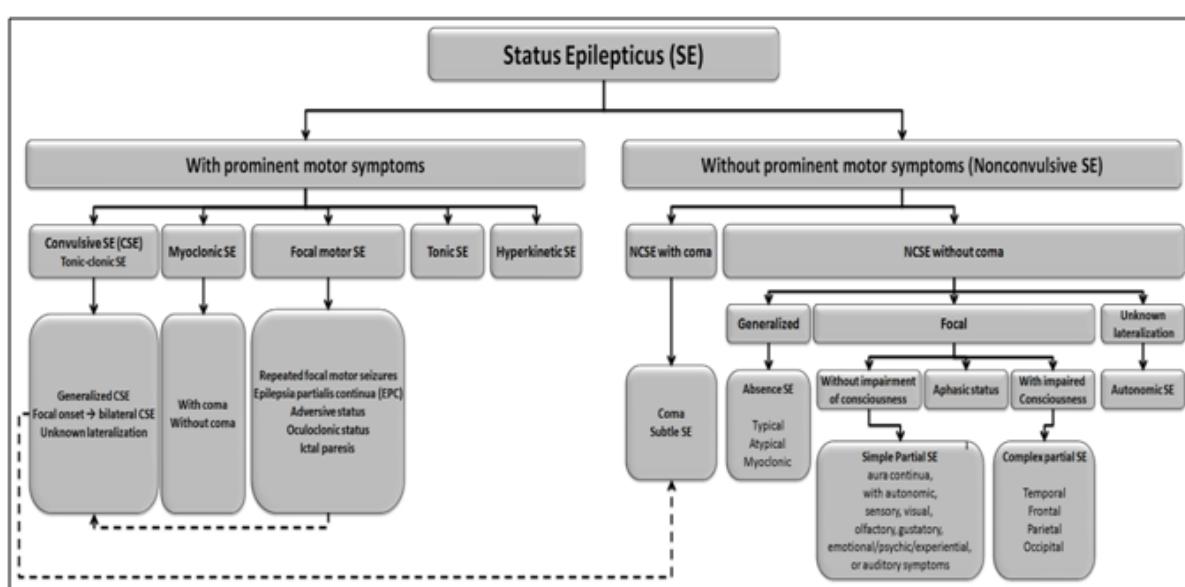
1. The presence or absence of prominent *motor symptoms*.
2. The degree (qualitative or quantitative) of *impaired consciousness*.
3. Etiology

Etiology can be classified as known common causes and unknown where a cause cannot be found. The term "known" or "symptomatic" is used for a known disorder, which can be structural, metabolic, inflammatory, infectious, toxic, or genetic⁶

Etiology

1. Known (symptomatic) Acute (e.g., stroke, intoxication, metabolic derrangements, encephalitis, etc.)

Remote (e.g., posttraumatic, postencephalitic, poststroke, etc.)



Progressive (e.g., brain tumor, Lafora's disease, dementias) SE in **defined electroclinical syndromes** 2. **Cryptogenic**

3 EEG correlates

Currently there are no evidence-based EEG criteria for SE. Based on large descriptive series and consensus panels^{7,8} these are terminologies to describe EEG patterns in SE:

1. **Location:** generalized (including bilateral synchronous patterns), lateralized, bilateral independent, multifocal⁷.
2. **Name of the pattern:** Periodic discharges, rhythmic delta activity or spike-and-wave/ sharp-and-wave plus subtypes.
3. **Morphology:** sharpness, number of phases (e.g., triphasic morphology), absolute and relative amplitude, polarity⁸.
4. **Time-related features:** prevalence, frequency, duration, daily pattern duration and index, onset (sudden vs. gradual), and dynamics (evolving, fluctuating, or static).
5. **Modulation and effect of interventions on EEG:** stimulus-induced vs. spontaneous⁸.

4) Age

Classification according to age helps to identify different etiologies in different age groups

1. Neonatal (0 to 30 days).
2. Infancy (1 month to 2 years).
3. Childhood (> 2 to 12 years).
4. Adolescence and adulthood (> 12 to 59 years).
5. Elderly (e" 60 years).

Younger population may be prone for genetic epilepsy syndromes. Older people tend to have trauma or stroke as leading etiologies.

Nonconvulsive status epilepticus (NCSE)

It is expected that most of the time, status epilepticus will manifest with motor symptoms but this entity has epileptic discharges in the brain

without motor manifestations . It was originally described in patients with chronic epilepsy, but increasingly recognized in the critically ill. The diagnosis and treatment of NCSE are not straightforward and depend on many variables, including the clinical setting and etiology, electroencephalography (EEG) findings, and the clinical status of the patient⁸.

2) Diagnosis and Assessment –

The diagnosis of GCSE depends on history and clinical examination. The diagnosis of convulsive status is confirmed by verifying the presence of either an unremitting generalized convulsive seizure lasting longer than five minutes or multiple bilateral convulsive seizures without an interictal return to the baseline level of consciousness.

URGENT FOCUSED EVALUATION

During early treatment, the clinician should obtain a focused history from a family member or caregiver.

History

1. Prehospital administration of benzodiazepines and any antiseizure medications (ASMs)
2. Past history of epilepsy or events
3. Acute illness or toxic substance like alcohol, illicit drugs
4. Medication history for similar or other illnesses
5. For patients with prior status epilepticus, history of treatment response to particular drugs.

A rapid neurologic examination should be performed to determine the type of status epilepticus and its etiology.

IMMEDIATE SUPPORTIVE CARE

The main goals of care are:

Like any other medical emergency,

1. Establish and maintain adequate **Airway, Breathing, and Circulation**

2. Stop the seizure with appropriate ASMs.
3. Identify and treat life-threatening causes such as trauma, sepsis, meningitis, encephalitis, or structural brain lesion

Patients with generalized convulsions should have continuous monitoring of

- a) Heart rate and rhythm
- b) Respiratory rate and pulse oximetry
- c) Periodic measurement of blood pressure and temperature.

Intravenous access should be secured immediately and blood drawn for following tests-

- a) Blood sugar
- b) Liver and renal function tests
- c) Sodium, potassium, calcium and magnesium levels
- d) Complete blood count
- e) Levels of antiseizure medications
- f) Urine pregnancy test in appropriate setting
- g) **Arterial blood gases once patient stabilizes**

Correction of hypoglycemia-

Every patient of status epilepticus should undergo checking of blood sugar levels at arrival in the emergency department. Hypoglycemia may provoke seizures and convulsive status epilepticus.

Correction of metabolic parameters

Hyponatremia, hypocalcemia may lead to seizures and some may progress to status epilepticus. Many patients also develop metabolic acidosis which needs correction.

Correction of hemodynamic parameters

Rapid evaluation of shock and prompt correction is needed. Underlying conditions like cardiogenic shock, trauma and acidosis may lead to hypotension. Prompt correction with IV colloids and crystalloids as indicated.

EMERGENCY ANTI-SEIZURE MEDICATIONS

First line therapy

Benzodiazepines are the first-line agents used for management of convulsive status epilepticus because they control seizures rapidly. Initial rapid termination of seizures leads to reduced chance of going into the next phase and use of multiple ASMs.

For the intravenous (IV) route, lorazepam is the preferred drug of choice.

Lorazepam 0.1 mg/kg should be administered intravenously at a maximum rate of 2 mg/minute. A practically easy guide in adults is initial loading dose of lorazepam 4 mg fixed dose, repeated if still seizing¹⁰.

If seizures continue after five minutes, additional doses of lorazepam can be infused at a maximum rate of 2 mg/minute.

If IV access is not possible, alternative routes of administration need to be considered.

Midazolam is preferred for intramuscular (IM), intranasal, or buccal administration.

IM midazolam is given as 10mg dose.

The typical dose of buccal midazolam is 0.2 mg/kg, or 10 mg in adolescents and adults. The dose of intranasal midazolam using the nasal spray formulation (5 mg/0.1 mL) is one spray (5 mg) in each nostril to give 10 mg.

Diazepam is preferred for rectal administration⁹. A typical dose of diazepam is 0.2mg/kg up to 20mg in an adult. Rectal diazepam is preferred in pediatric population.

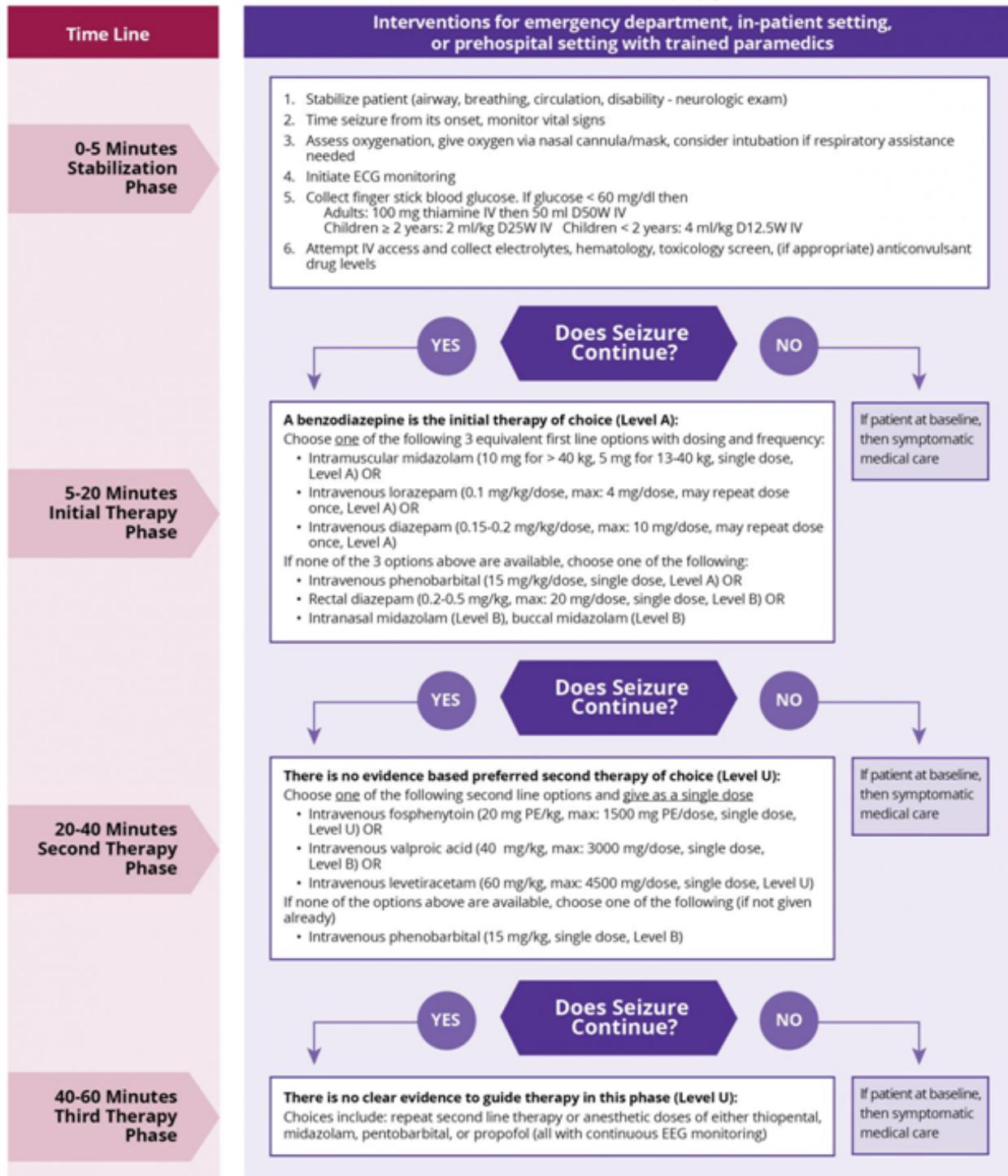
After initial 5-20 minutes if seizures do not stop with benzodiazepine administration, one of the antiseizure medications need to be administered.

Second line therapy

Even if the initial seizures have ceased with first line agents, they are short acting and mostly need a second line antiseizure to further prevent recurrence. If a correctable cause like hypoglycemia

Proposed Algorithm for Convulsive Status Epilepticus

From "Treatment of Convulsive Status Epilepticus in Children and Adults," *Epilepsy Currents* 16.1 - Jan/Feb 2016



Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytic framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate.

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is found then second line agent may not be needed. Most of the times, a second line agent is administered after first line therapy.

Administration of second line ASMs should be weight based for the desired effect. The selection of agent is as per patient comorbidities, the drug safety, potential side effects, comfort of the physician and availability of drugs.

Traditionally, phenytoin or fosphenytoin has been used as a first line agent. However, levetiracetam and valproate are also used as first line agents now when clinically appropriate^{9,10}. All three agents are considered effective as first line in adequate per kg dosing.

If patient is on a subtherapeutic dosing of a particular agent, the same agent may be repeated at therapeutic dose. If a patient is having seizure recurrence while taking one agent, another agent may be preferred. If a patient has renal or liver dysfunction, levetiracetam is the preferred agent.

Comparative studies to demonstrate seizure cessation, return of consciousness and long-term outcome have shown equal effectiveness of fosphenytoin, levetiracetam and valproic acid¹¹.

Fosphenytoin – Fosphenytoin is the generally preferred formulation of phenytoin for rapid intravenous dosing. The loading dose is 20 mg / kg, infused at a rate of 100 to 150 mg /minute. Cardiac monitoring and frequent vital signs are required during the infusion of fosphenytoin or phenytoin and for at least 15 minutes.

Phenytoin – Phenytoin is generally started with a loading dose of 20 mg/kg, infused at a rate of up to 50 mg/minute. In addition, the risks of local pain and injury (including venous thrombosis and the rare purple glove syndrome) increase with more rapid infusions. Cardiac monitoring during the initial infusion is mandatory because cardiac arrhythmias may occur¹⁰.

Levetiracetam — A loading dose of 60 mg/kg IV in adults (maximum 4500 mg) infused over 5 to 15 minutes¹¹

Levetiracetam is increasingly used as the second

line ASM due to its lack of interactions with other drugs and overall excellent tolerability and side effect profile.

Valproate — Intravenous valproate is increasingly used in the treatment of status epilepticus. It is preferred over phenytoin in patients with primary generalized epilepsies who develop status epilepticus. It is particularly useful as a nonsedating option in patients with focal or myoclonic status epilepticus (MSE).

A loading dose of 40 mg/kg can be infused safely at a rate of 10 mg/kg per minute (maximum dose 3000 mg) in adults without adverse effects on blood pressure or heart rate¹¹.

The risk of hepatic toxicity and hyperammonemic encephalopathy due to valproate may pose diagnostic challenge in post ictal phase¹².

Third-line therapy — There are several antiseizure medications that can be useful in the management of status epilepticus.

Phenobarbital and lacosamide can be given intravenously and may be particularly useful as adjunctive agents in patients with focal or nonconvulsive status epilepticus, as an additional treatment in patients with refractory status epilepticus.

Phenobarbital –

Initial doses of phenobarbital 20 mg/kg infused at a rate of 30 to 50 mg/minute are generally used.

Lacosamide – Accumulating data indicate that IV lacosamide (200 to 400 mg IV bolus) is usually well tolerated and may have similar efficacy compared with other agents used to treat refractory status epilepticus^{9,11}. An ECG should be performed before use of lacosamide and during maintenance to monitor for PR prolongation¹¹.

Refractory Generalized convulsive status epilepticus (GCSE)

Adequate and optimal treatment of GCSE with benzodiazepines and antiseizure medications is completed within 10 to 20 minutes. In patients with GCSE who are actively seizing at 30 minutes

despite two initial doses of a benzodiazepine and administration of one or two other ASM loads, preparation for a continuous infusion of midazolam, propofol, or pentobarbital should begin.

Before starting anesthetic agents, at this stage, the patient will need endotracheal intubation and mechanical ventilation if not done before. Patient needs to be transferred to neurology ICU and needs continuous EEG monitoring^{1,2}.

Focal motor status epilepticus — Most focal status epilepticus cases are treated with the same antiseizure medications as for GCSE²

Super-refractory status epilepticus- Despite use of benzodiazepines, 2 or more antiseizure medications and anesthetic agents as per protocol, if the seizures still persist beyond 24 hours, it is termed as super refractory¹³.

Variable agents have been tried in this case like ketamine, steroids, magnesium and other anesthetic agents¹³.

New terminology

NORSE- New onset refractory status epilepticus

It is defined as a status epilepticus which comes out of the blue as a first-time presentation and is refractory to standard treatment options. In children this condition if preceded by fever or viral illness is called **FIREs**(Fever induced refractory status epilepticus) -a subtype of NORSE¹⁴.

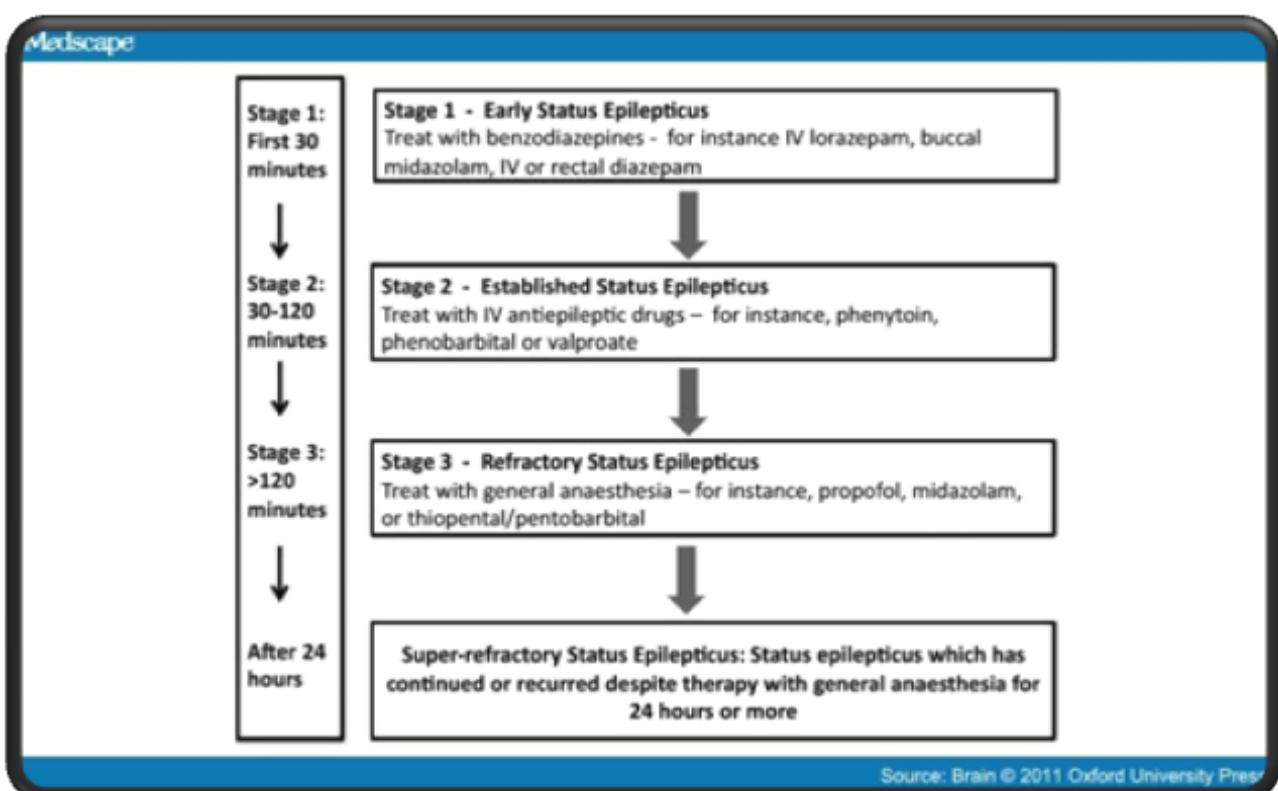
Usually, a cause like stroke, infection, structural or metabolic abnormality is not found. NORSE is said to be secondary to some viral illness triggered autoimmune process leading to encephalitis and seizure. Workup for antibodies and lumbar puncture study sometimes show certain autoimmune marker positivity.

In most of the cases no known cause is found and is termed as **Cryptogenic NORSE**¹⁴.

POSTICTAL RECOVERY AND FURTHER EVALUATION

Expected pace of recovery —

It is expected that patients start regaining consciousness after 10-30 minutes of a seizure.



However, that duration may be prolonged due to medications or ongoing non convulsive status epilepticus.

Neurologic examination —After the seizures are controlled, repeated detailed neuro examination and GCS monitoring is warranted. Also, if GCS is dropping assessment of non-convulsive state of SE should be done. For this a continuous EEG monitoring needs to be done.

EEG monitoring

All patients with seizures or status epilepticus who do not return to a normal level of consciousness after initial treatment should be monitored by cEEG to determine whether seizures are controlled.

Neuroimaging — Patients with new onset seizure presenting as status and those with focal neuro signs need to undergo an imaging. Patients with known epilepsy syndromes may not need imaging immediately.

MRI or CT scan may be planned as per suspected etiology. CT scan of brain is better for evaluation of trauma or when immediate structural lesion needs to be ruled out. MRI is better for evaluation of etiology.

Lumbar puncture – Patients with suspected neuro infection or intracranial metastasis based on imaging study need to undergo lumbar puncture for CSF analysis.

6) Conclusion

Despite more than three decades of rigorous research and clinical studies, up to 40% of patients in early status cannot be controlled with first line drugs. The treatment of super-refractory status is still an almost evidence free zone¹³. As more and more new antiseizure medicines are being introduced, research is underway to study their efficacy, tolerability in status patients. The management of status epilepticus is evolving and each country and institute may follow their own protocols based on medication availability, experience and available intensive care.

References

1. Wirrell E, Tinuper P, Perucca E, Moshé SL. Introduction to the epilepsy syndrome papers. *Epilepsia*. 2022;63:1330–1332.
2. Trinka, E., Cock, H., Hesdorffer, D., Rossetti, A.O., Scheffer, I.E., Shinnar, S., Shorvon, S. and Lowenstein, D.H. (2015), A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus. *Epilepsia*, 56
3. Shinnar S, Berg AT, Moshe SL, et al. How long do new-onset seizures in children last? *Ann Neurol* 2001;**49**:659–664
4. Engel J Jr, International League Against Epilepsy (ILAE). A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 2001;**42**:796–803.
5. Bauer G, Trinka E. Nonconvulsive status epilepticus and coma. *Epilepsia* 2010;**51**:177–190.
6. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia* 2010;**51**:676–685.
7. Hirsch LJ, LaRoche SM, Gaspard N, et al. American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version. *J Clin Neurophysiol* 2013;**30**:1–27
8. Sutter R, Kaplan PW. The neurophysiologic types of nonconvulsive status epilepticus: EEG patterns of different phenotypes. *Epilepsia* 2013;**54**(Suppl. 6):23–27.
9. Silbergliit R, Durkalski V, Lowenstein D, Conwit R, Pancioli A, Palesch Y, Barsan W; NETT Investigators. Intramuscular versus



intravenous therapy for prehospital status epilepticus. *N Engl J Med.* 2012 Feb 16;366(7):591-600

10. Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, Laroche SM, Rivelli JJ Jr, Shutter L, Sperling MR, Treiman DM, Vespa PM; Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care.* 2012 Aug;17(1):3-23
11. Kapur J, Elm J, Chamberlain JM, Barsan W, Cloyd J, Lowenstein D, Shinnar S, Conwit R, Meinzer C, Cock H, Fountain N, Connor JT, Silbergliit R; NETT and PECARN Investigators. Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus. *N Engl J Med.* 2019 Nov 28;381(22):2103-2113.
12. Rossetti AO, Bromfield EB. Efficacy of rapid IV administration of valproic acid for status epilepticus. *Neurology.* 2005 Aug 9;65(3):500-1
13. Trinka E, Kälviäinen R. 25 years of advances in the definition, classification and treatment of status epilepticus. *Seizure.* 2017 Jan;44:65-73.
14. EPIGRAPH VOL. 22 ISSUE 4, SUMMER 2020.Understanding new-onset refractory status epilepticus (NORSE): Awareness and research;ILAE



Upper GI Bleed – Approach and Management

Dr Sreekanth Appasani

Consultant Interventional Gastroenterologist & Therapeutic Endoscopist,
KIMS Hospital, Secunderabad.
Shine Gastro Centre, KPHB Colony, Hyderabad.

INTRODUCTION

Upper Gastrointestinal (GI) bleed is defined as any bleed occurring proximal to ligament of Treitz. Commonest presentation is hematemesis (vomiting of blood or coffee-ground-like material) and/or melena (black, tarry stools). It is a common medical emergency and has a mortality rate of around 10%. The incidence and mortality markedly increase with age. Higher importance should be given to simultaneous resuscitation, investigation, and active monitoring of the acutely bleeding patient than for interventions since early intervention in an unstable patient could be detrimental. Decompensation of underlying cardio-pulmonary, renal and liver issues with poorly tolerated shock remains the main cause for death in this clinical scenario. Important goal is to stop continuing hemorrhage and decrease

the risk of rebleed. New endoscopic techniques, emergence of interventional radiological techniques in collaboration with surgery have decreased the morbidity and mortality in the recent era.

ETIOLOGY

Upper GI bleed could be variceal or non-variceal causes. Common causes of non-variceal bleed are peptic ulcer/erosions, esophagitis, Mallory Weis tear, angiodysplasia and malignancies. Various causes have been classified and summarized in table 1. Variceal bleed (25% of upper GI bleeds) could occur from esophagus, fundus of stomach or ectopic sites like duodenum, small bowel also. Peptic ulcer disease (50% of upper GI bleeds) forms the most common cause of GI bleed in all ages, more in elderly age. With the advent of extensive proton pump inhibitor

Table 1 : Causes of Upper GI bleed

Esophagus	Stomach	Duodenum
1. Esophageal varices	1. Gastric varices	1. Peptic Ulcer Disease
2. Malignancy	2. Ulcers	2. Erosions
3. Esophagitis	3. Erosions	3. Hemobilia
4. Mallory Weis tear	4. Malignancy	4. Hemosuccus pancreaticus
5. Aorto-enteric fistula	5. Dielafuoy lesion	5. Malignancy
6. Esophageal ulcers	6. Gastric Antral Vascular Ectasia	6. Dielafuoy lesion
7. Corrosive injury	7. Portal hypertensive gastropathy	7. Portal hypertensive duodenopathy

usage, the incidence is albeit decreasing. *H. pylori* infection, NSAID's & Aspirin usage contribute to most common reasons for peptic ulcer disease. Esophagitis is also a form of peptic ulcer disease but causes minor bleeding unless a large vessel is involved. Malignancies also present with smaller bleeds due to surface ulceration, however gastrointestinal stromal tumours can present with massive bleeds due to high vascularity. The Dieulafoy's lesion is a ruptured, thick-walled artery with little or no associated ulceration, commonly seen in fundus of stomach, also seen in duodenum and other parts of small intestine. Telangiectasias also are another form of arterio-venous malformations which could bleed, commonly seen in renal impairment patients and aged population.

INITIAL EVALUATION

Initial evaluation of a patient with suspected acute upper GI bleed includes a history, physical examination, and laboratory tests. The goal of the evaluation is to assess the severity of the bleed, identify potential sources of the bleed, and determine if there are conditions present that may affect subsequent management. The information gathered as part of the initial evaluation is used to guide decisions regarding triage, resuscitation, empiric medical therapy, and diagnostic testing.

Symptoms : Presence of hematemesis or coffee ground vomitings, melena suggests upper GI bleed. Blood as little as 50-80ml can cause melena and can persist for 1 week after an initial bleed episode. Hematochezia (fresh blood or maroon-colored stools) usually is seen in lower GI bleed but can be seen also in massive upper GI bleed with rapid transit. Usually, patients have orthostatic hypotension or hemodynamic compromise in such situation. In the absence of overt bleed, symptoms that suggest bleeding are severe include orthostatic dizziness, confusion, angina, severe palpitations, and cold/clammy extremities.

History : History of previous peptic ulcer disease, liver disease, alcohol abuse, NSAID, Aspirin, antiplatelet or anticoagulant usage is necessary to predict the cause of bleed. Comorbid illness like renal or cardiac should be taken into

consideration since they influence the cause as well as outcome of bleed. Also, these comorbid illness determine the aggressiveness of resuscitation since overload needs to be avoided while adequate transfusions and fluids are given

- Abdominal pain might suggest peptic ulcer disease, could be seen with other etiologies too.
- Presence of jaundice, abdominal distension, pedal edema could suggest chronic liver disease and variceal cause.
- Presence of odynophagia, dysphagia, reflux could suggest esophagitis/ulcer.
- Presence of early satiety, involuntary weight loss, cachexia, dysphagia, vomitings could suggest malignancy.
- Presence of severe retching or cough with vomitings could suggest Mallory Weis tear.
- Previous vascular surgeries, grafts for aortic aneurysms suggest a life threatening aorto-enteric fistula.
- Lastly be aware of drugs and supplements which can cause black stools like iron, bismuth, and charcoal.

EXAMINATION

The physical examination involves general findings similar to other cases which could point towards the etiology of bleed like jaundice, ascites, abdominal lump, etc. However a key component of the assessment is hemodynamic stability because it guides both treatment pace and direction. Pulse rate and blood pressure forms the most important predictor for hemodynamic instability unless influenced by external factors like beta blockers, etc. Hypovolemia due to blood loss can be predicted as below :

- Resting tachycardia : Blood volume loss less than 15%
- Orthostatic hypotension : Blood volume loss of at least 15% (a decrease in the systolic blood pressure of more than 20 mmHg

and/or an increase in heart rate of 20 beats per minute when moving from recumbency to standing)

- Supine hypotension : Blood volume loss of at least 40%

Nasogastric lavage may be carried out for two reasons : confirmation of upper GI bleed and aiding endoscopic visibility for therapeutic intervention. It is not a sensitive or specific test and few studies have suggested increased aspiration risk but it's a commonly performed procedure in all upper GI bleeds in emergency triage area and is recommended. An alternative to naso-gastric lavage to improve visibility is to use a prokinetic such as metoclopramide, levosulpiride, erythromycin. If severe abdominal pain with rebound tenderness or guarding is noted, perforation needs to be ruled out and a cross sectional imaging modality like CT should be done before contemplating endoscopy.

LABORATORY DATA

As in every admission from emergency department, routine blood work like complete blood count, serum chemistries, liver tests, coagulation studies and a blood gas analysis need to be done. In addition, electrocardiograms, 2D echocardiogram, cardiac enzymes may be indicated in selected patients who are at risk for cardiac dysfunction. Hemoglobin may be falsely stable in initial presentation since whole blood is

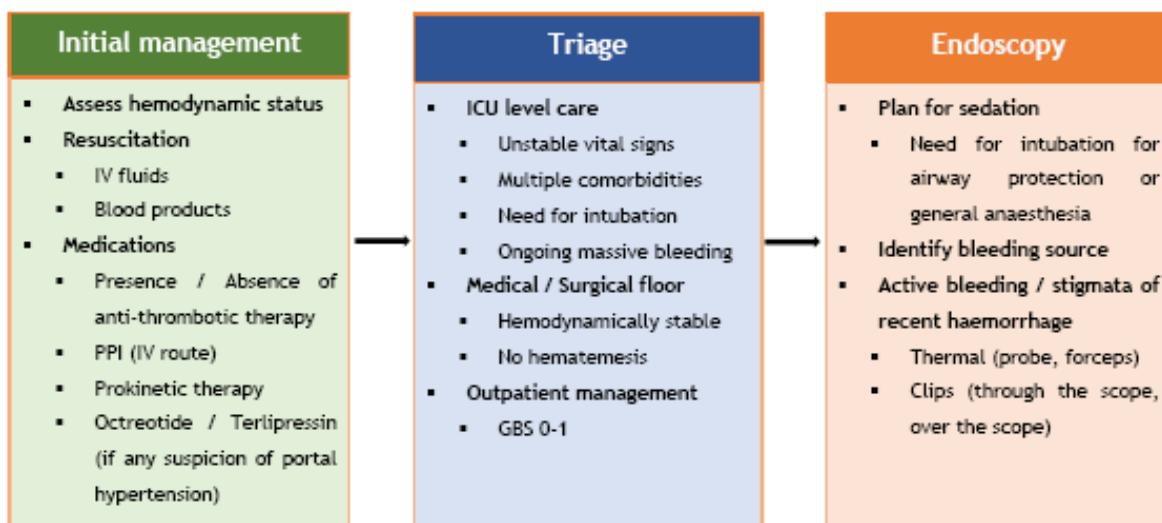
lost and hematocrit is elevated due to volume loss, however with time, the hemoglobin level will decline as the blood is diluted by the influx of extravascular fluid into the vascular space and by fluid administered during resuscitation. The hemoglobin level should initially be monitored every four to eight hours, until stabilized. Blood urea may also be elevated without renal dysfunction since blood is absorbed when it passes from small bowel and urea from blood metabolism re-enters the circulation.

GENERAL MANAGEMENT

The multidisciplinary team should be informed at an early stage and this might include gastroenterologists, surgeons, anaesthetists and the critical care team.

Supportive care : Patients with hemodynamic instability noted by shock, orthostatic hypotension should be triaged preferentially and treated aggressively. Nil by mouth is the strategy for all patients until stabilization and confirmation of therapy by endoscopy. Provide supplemental oxygen (goal oxygen saturation >94% for patients without COPD). Elective endotracheal intubation in patients with ongoing hematemesis or altered respiratory or mental status decreases the risk of aspiration protecting the airway and also facilitates a better endoscopy.

Intravenous access : Adequate peripheral access with either two 18 gauge or larger intravenous



catheters and/or a large-bore, single-lumen central venous access to be obtained.

Fluid resuscitation : This is one most important treatment modality which saves the patient in initial golden hours. Begin immediately, do not delay pending transfer to intensive care unit. Treat hypotension initially with rapid, bolus infusions of isotonic crystalloid (eg, 500 to 1000 mL per bolus; normal saline or ringer lactate; use smaller boluses and lower total volumes for patients with compromised cardiac function). If patient fails to respond to fluid resuscitation, temporary support with vasopressor drugs may be required. Adequate resuscitation and hemodynamic stabilization is essential prior to endoscopy to minimize treatment-associated complications. Patients at risk of fluid overload may require intensive monitoring.

Transfusion : Do not wait for haemoglobin report if a patient is actively bleeding and pouring out blood.

- For severe, ongoing bleeding, immediately transfuse blood products in 1:1:1 ratio of RBCs, plasma, and platelets, as for trauma patients. Use a restrictive transfusion strategy.
- Threshold for transfusion in cardiac and elderly patients should be <8gm/dL, in low-

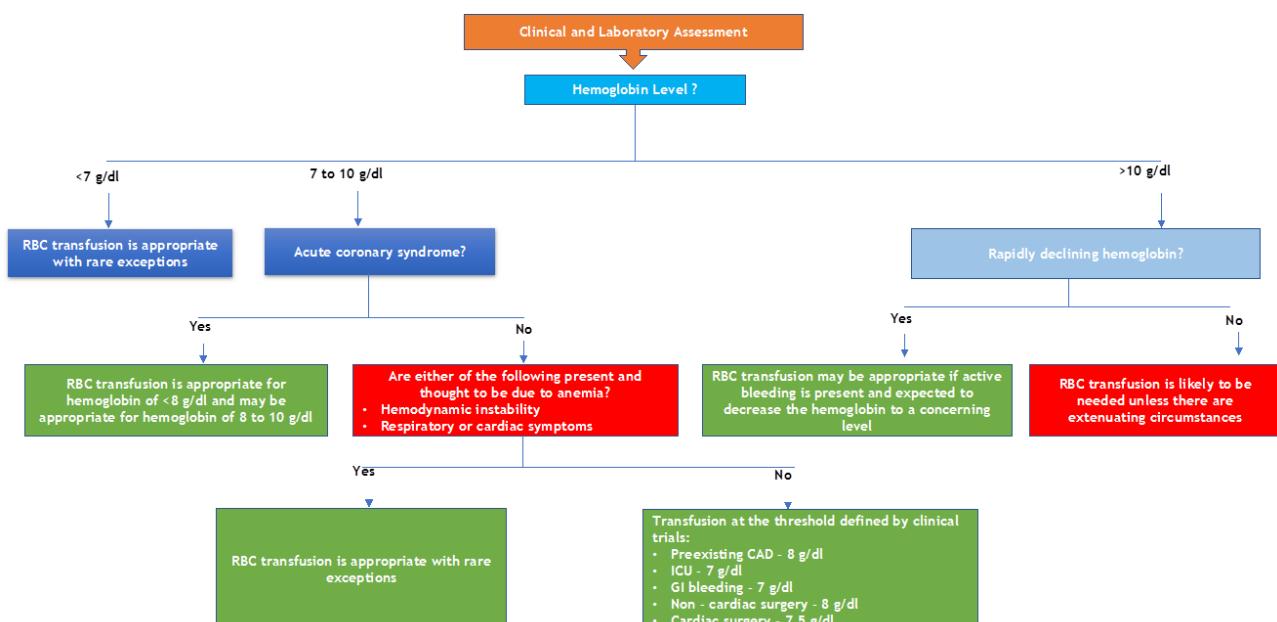
risk patients it should be at 7gm/dL.

- Give plasma after every 4 units of RBC transfusion and for correcting coagulopathy.
- Give platelets for thrombocytopenia (<50,000/mL), after every 4 units of RBC transfusion, suspected platelet dysfunction or on antiplatelet therapy.
- Avoid over transfusion if variceal bleed is suspected (threshold to be < 7gm/dL), since portal pressures will increase with over transfusion leading to rebleed or worsening of existing bleed.
- Massive transfusions (>3 in an hour, >10 in 24 hrs) will need plasma and platelet replacement.

Red blood cell (RBC) transfusion decisions in adults

Correction of coagulopathy, dealing with reversal and antiplatelets :

In active GI bleed, stop all medications dealing with coagulation and platelets. Endoscopy should be done irrespective of coagulation levels in such situations, however in a hemodynamically stable patient, its better to wait until INR < 2.5, since its safe and endotherapy is more effective. In patients with severe, ongoing bleeding who are taking an



anticoagulant, administration of a reversal agent might be necessary and need to be individualized. Medications of such nature can be restarted once the bleeding has been treated endoscopically to prevent a thrombotic event. In high-risk cases like recent stroke or myocardial infarction, where anticoagulation or antiplatelets are necessary, they could be restarted carefully after bleed control has been. Other hematological conditions could be dealt in coalition with a hematologist.

RISK STRATIFICATION AND TRIAGE

It is important for patients to be triaged into high risk or low risk category for optimization and channeling of treatment. All high-risk patient marked by with hemodynamic instability or active bleeding should be admitted to an intensive care

unit for resuscitation and close observation with blood pressure monitoring, electrocardiographic monitoring, and pulse oximetry. Other low risk patients who are hemodynamically stable can be admitted to a regular ward. Outpatient management may be appropriate for some low-risk patients with no stigmata of bleed even on endoscopy. Instead of these subjective assessments, in clinical practice it is mandatory to use scoring systems such as the Glasgow-Blatchford score, Rockall score or AIMS-65 score for triage. Scores of 0 or 1 could suggest low risk patients and increased scores triggers a high-risk patient. Rockall score uses endoscopic data also, hence more robust. However, in emergency department, Glasgow Blatchford score and AIMS scores could be used without endoscopic data.

ROCKALL RISK SCORE				
Score Variable	0	1	2	3
Age (Yrs)	<60	60-79	>80	
Shock	No shock	SBP > 100 mm Hg HR < 100 bpm	Tachycardia SBP > 100 mm Hg HR > 100 bpm	Hypotension SBP < 100 mm Hg
Comorbidity	No major comorbidity		CCF, IHD, Major Comorbidity	Renal failure, Liver failure, Disseminated malignancy
Diagnosis	Mallory Weis Tear, no lesion identified, no SRH	All other diagnosis		
Major SRH	None or dark spot only		Blood in upper GI tract, adherent clot, visible vessel, spurting vessel	

CCF - congestive heart failure, IHD - ischemic heart disease, SBP - systolic blood pressure, HR - heart rate

GLASGOW-BLATCHFORD SCORE	
Admission Risk Factor	Score Component Value
Blood urea (mmol/L)	
≥ 6.5 < 8.0	2
≥ 8.0 < 10.0	3
≥ 10.0 < 25.0	4
≥ 25	6
Hemoglobin (g/L) for men	
≥ 12.0 < 13.0	1
≥ 10.0 < 12.0	3
< 10.0	6
Hemoglobin (g/L) for women	
≥ 10.0 < 12.0	1
< 10.0	6
Systolic Blood Pressure (mm Hg)	
100-109	1
90-99	2
< 90	3
Other markers	
Pulse ≥ 100 (per min)	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

AIMS-65 SCORE	
Admission Risk Factor	Score Component Value
Albumin (mg/dL)	
> 3	0
< 3	1
INR	
< 1.5	0
> 1.5	1
Mental status	
Normal	0
Altered	1
Systolic Blood Pressure (mm Hg)	
> 100	0
< 100	1
Age (years)	
< 65	0
> 65	1

MEDICATIONS

Acid suppression :

Proton pump inhibitors play an important role in GI bleed management, especially upper GI bleeds. Mechanism of action includes clot stabilization due to neutralization of gastric acid and achieving good internal milieu for preventing rebleed. They also promote hemostasis in patients with lesions other than ulcers. Optimal dosing would be to give an high dose intravenous bolus of 80mg, followed by intravenous infusion of 8mg/hr. Alternative to infusion, could be 40mg intravenously 12hrly or 6hrly depending on the severity of initial bleed and endoscopic findings predicting recurrence of bleed. Esomeprazole is slightly more efficacious than omeprazole and pantoprazole, however in emergency setting, either could be used based on availability. After patient stabilization and transfer to ward, either intravenous or oral proton pump inhibitor could be used depending on rebleed risk. If low risk for rebleed on endoscopy, oral formulation could be sufficient expediting early discharge. H2 receptor antagonists are not recommended due to inferior acid suppressive capacity in the setting of upper GI bleed. To summarize, oral and intravenous PPI therapy stabilizes the clot, reduces rebleeding rate, decreases the length of hospital stay, and need for blood transfusion, especially in patients with high-risk ulcers even after treatment with endoscopic therapy

Prokinetics :

The goal of using a prokinetic agent is to improve gastric visualization at the time of endoscopy by clearing the stomach of blood, clots, and food residue. Erythromycin, Metoclopramide have been used since long time to achieve this scenario. For erythromycin, a reasonable dose is 250 mg intravenously over 20 to 30 minutes. It acts on motilin receptors to create a prokinetic effect. Patients receiving erythromycin need to be monitored for QTc prolongation. Endoscopy is performed 20 to 90 minutes following completion of the erythromycin infusion. Metoclopramide could also be used for similar effect; dosage could

start with 10mg slow bolus up to 1mg/kg as an infusion by dilution in saline. Recent drugs like Levosulpiride 75mg also could be given as an intravenous bolus to achieve a good prokinetic action. Metoclopramide and Levosulpiride have extra-pyramidal side effects and usage should be judicious in high-risk patients. Erythromycin is a cytochrome P450 3A inhibitor, so drug interactions should be considered.

Vasoactive medications :

Vasoactive drugs like Octreotide, Somatostatin and Terlipressin have an important role in management of variceal bleed, in non-variceal bleed also it could have an adjunctive role by reducing the severity of bleed. Mechanism of action includes splanchnic vasoconstriction leading to reduced bleeding. Octreotide dosage is 50mcg bolus followed by 50mcg/hr infusion. Somatostatin dosage is 250mcg bolus dose followed by 250mcg/hr infusion. Terlipressin dose is 2mg bolus dose followed by 1mg every 4-6 hrly. Both Octreotide and Somatostatin need intravenous infusion after dilution in saline, Terlipressin could be given as slow intravenous infusion. Blood sugar monitoring is necessary with octreotide and somatostatin infusions since they effect the insulin-glucagon secretions. Terlipressin has effect on myocardial circulation due to highly efficacious vaso-contraction; causes bradycardia, angina and could precipitate myocardial infarction, hence to be used cautiously in cardiac patients.

Antibiotics :

GI bleed patients are at increased risk of bacterial infections up to 20% in cirrhosis. Mechanism of infection is breach of gut barrier due to bleeding site disruption of mucosa and its defense mechanisms. This infection could initiate a cascading effect on the already kick-started inflammatory response in patients with cirrhosis and other major comorbidities. Hence there is a definite role for prophylactic intravenous antibiotics, right from the triage timing to achieve an overall reduction in infectious complications and possibly decreased mortality. A broad-spectrum antibiotic like Cefotaxime or Ceftriaxone

could be sufficient in routine patients. In patients with multiorgan failure, higher level antibiotics could be determined as per patients general condition and other determinants like sepsis, shock, renal impairment, etc.

Ineffective treatments :

Tranexamic acid is an antifibrinolytic agent that enhances clot stability by preventing its breakdown. Multiple studies and meta-analysis have concluded no mortality benefit even though some clinical effect on rebleed was noted. In contrary, some data suggests an increase in venous thromboembolic events (deep vein thrombosis, pulmonary embolism) and seizures. Hence it better to avoid using such agents of borderline benefit and some increased risk.

SPECIALIST INVOLVEMENT

Gastroenterology consultation is mandatory for all GI bleeds, since active endoscopic therapy would be contemplated for all patients irrespective of the risk. Surgical and interventional radiology consultation should be obtained if endoscopic therapy is unlikely to be successful, if the patient is deemed to be at high risk for rebleeding or complications associated with endoscopy, or if there is concern that the patient may have an aorto-enteric fistula. Surgical consultation is also necessary to appraise them of a potential emergency case to plan the OR schedule in case the endoscopic therapy fails. Interventional radiology consultation should be done for intervention like angiography +/- embolization. Hematologist to be involved in all patients with special coagulopathy conditions and in situations where coagulopathy is not being corrected despite routine infusions and interventions. Cardiology and nephrology consultations are deemed necessary as per patient's clinical situation. Wherever antiplatelets and anticoagulation was used and has been stopped due to GI bleed, corresponding clinician who started the treatment should be involved in clinical management specially during restart of medications.

DIAGNOSTIC STUDIES

Common investigations used are upper, lower and small bowel endoscopy in identifying and treating the bleed source. CT abdomen with angio protocol along with Technetium labelled RBC scan could be used if the bleed is obscure – either occult or overt. Following is an algorithm providing an overview of the diagnostic approach.

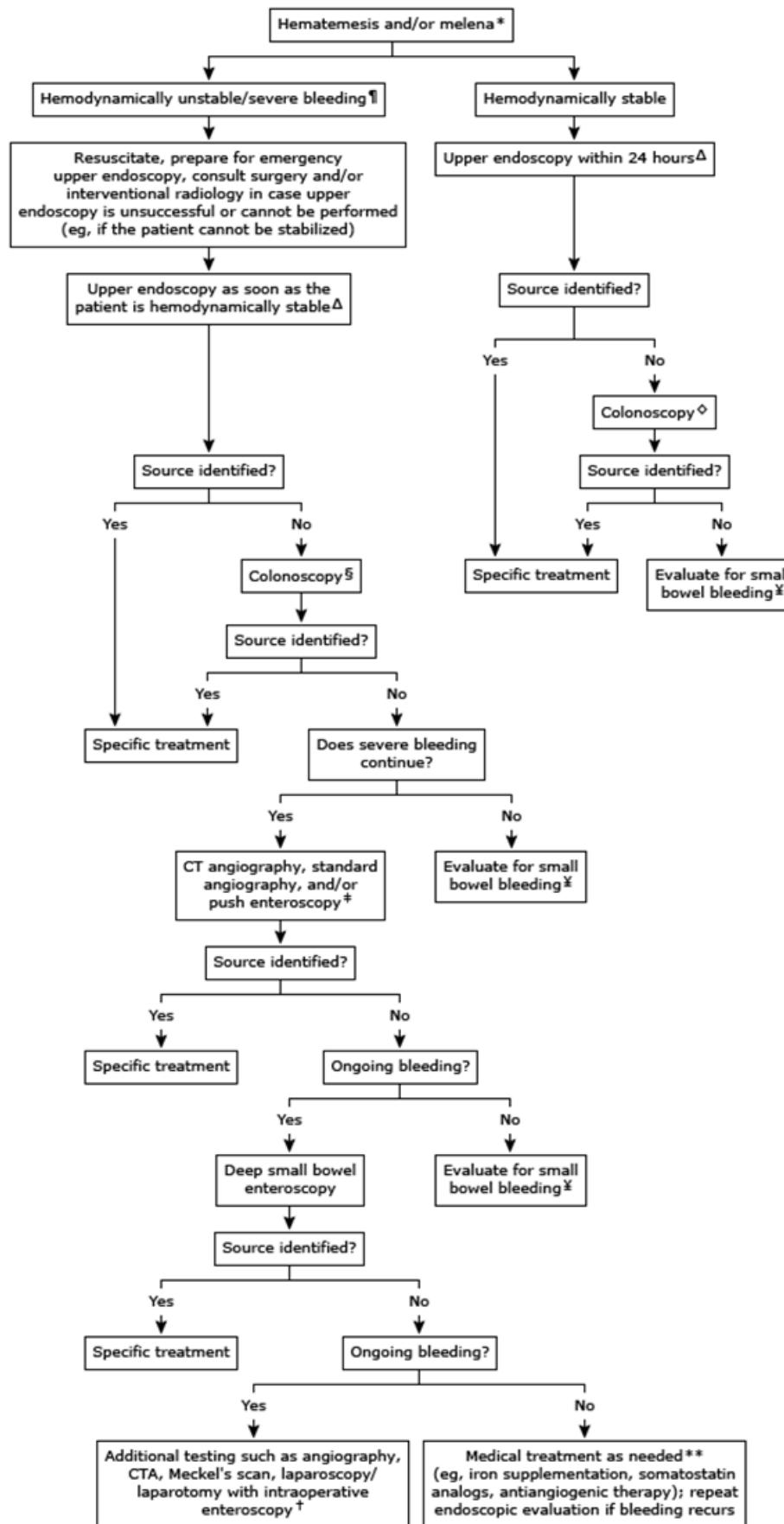
Upper endoscopy :

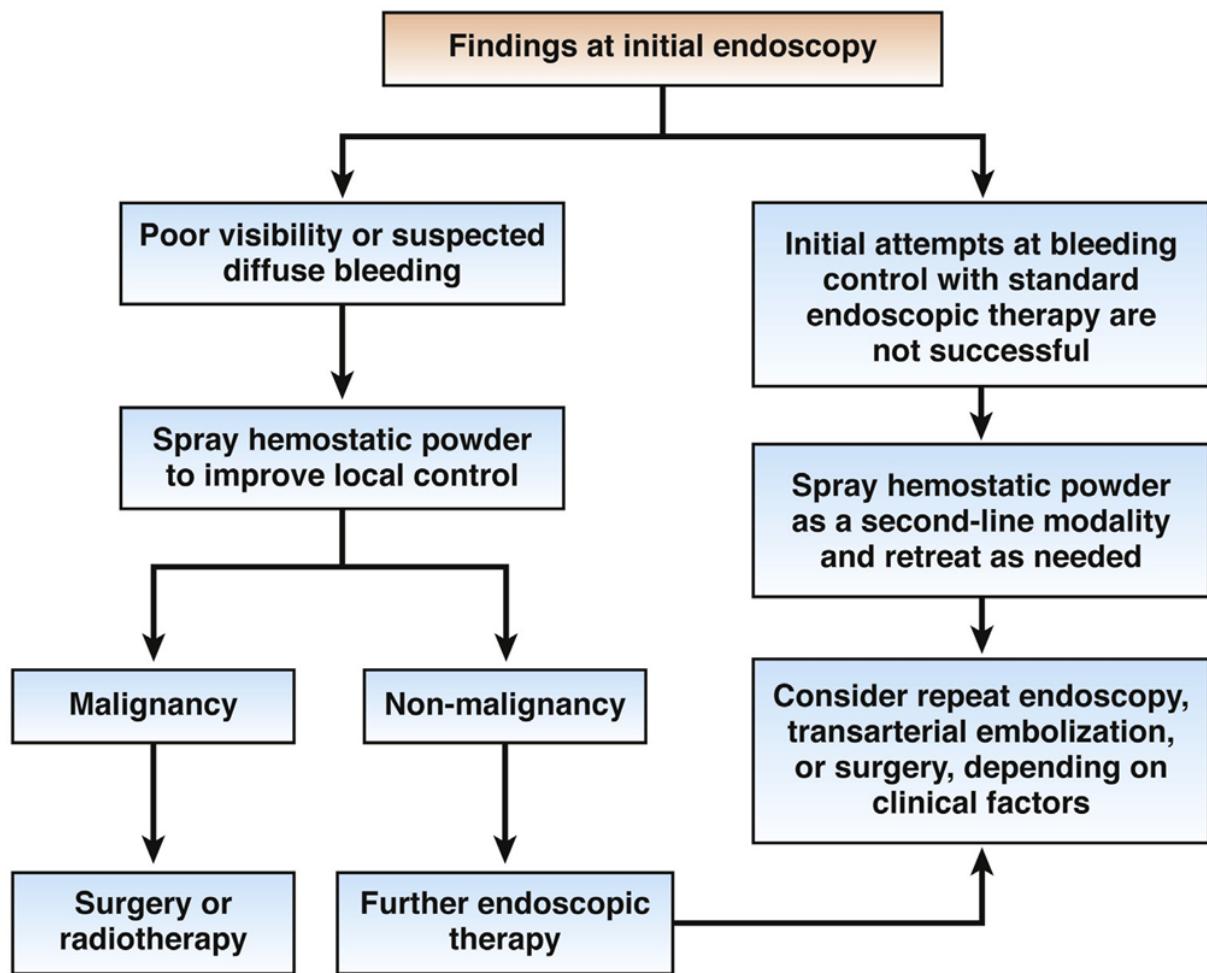
Endoscopy is the diagnostic modality of choice for acute upper GI bleeding. Endoscopy localizes and aids in treating the bleeding lesions in the upper GI tract with the highest sensitivity and specificity. It may be beneficial to give a prokinetic agent before endoscopy to enhance the visibility. An early endoscopy (within 24 hours) is recommended for most patients with acute upper GI bleeding to have a favorable outcome. In some situations like variceal bleed, we perform endoscopy within 12 hrs also. If ongoing bleed is noted, emergency endoscopy after taking care of airway, breathing and circulation might be necessary.

In variceal bleed, endoscopic band ligation is necessary to control the bleed. Advantage of band ligation is that if varices are confirmed, we can ligate the exact bleeding point with active bleed or stigmata like redo red or white nipple sign. If we can't identify these, a blind band ligation of varices in a spiral way starting from EG junction upwards could save the patient. In fundal varices, endoscopic glue injection is the treatment of choice. Patients with large varices might need repeat glue injection into non bleeding varices after treatment of bleeding varix, since large volume single injection could risk fatal pulmonary embolism.

In non-variceal bleed, peptic ulcers form the most common lesion identified. Forrest classification is applied to grade the findings to predict rebleed rate for triage as shown in the table below.

Endoscopic stigmata of recent hemorrhage





Endoscopic methods for hemostasis of non-variceal hemorrhage	
Method	Delivery
Thermally active methods	Electrocoagulation - Bipolar, Monopolar
	Heater probe
	Argon plasma coagulation
	Laser
Injection	Adrenaline 1:10000
	Tissue glues
Mechanical methods	Endoscopic clips - Over the scope
	Endoscopic clips - Through the scope
	Band ligation
Combination methods	Injection + Thermal
Newer methods	Special nano powder sprays

Endoscopic stigmata of recent hemorrhage	Risk of rebleeding	Endoscopic treatment
Forrest Ia - Active arterial bleeding	55%	Yes
Forrest Ib - Oozing without visible vessel	55%	Yes
Forrest IIa - Non-bleeding visible vessel	44%	Yes
Forrest IIb - Adherent clot	22%	Yes
Forrest IIc - Flat spot	10%	No
Forrest III - Clean ulcer base	5%	No

Early endoscopy, relook endoscopy :

Early endoscopy evaluates and treats a patient efficiently but only after adequate resuscitation has been provided. Urgent endoscopy (< 6hrs) may be associated with poor outcomes possibly due to inadequate resuscitation. Relook endoscopy has not been proven to be beneficial in trials but is commonly contemplated as per patient risk stratification. Relook endoscopy is mandatory if bleeding lesion is not identified in the index procedure. However if lesion is identified and therapy has been done, a routine relook endoscopy can be done after 48hrs to assess the adequacy and rebleed risk identification. In low risk patients where endotherapy was not done, relook endoscopy could be avoided.

Risks of endoscopy :

Risks of upper endoscopy include pulmonary aspiration, adverse reactions to medications used to achieve conscious sedation, GI perforation, and increasing bleeding while attempting therapeutic intervention. Most of them could be potentially avoided if adequately resuscitated prior to endoscopy and airway has been secured.

Other diagnostic tests :

If endoscopy is inconclusive or doesn't have significant findings to localize bleed, a CT

angiography is necessary – both to diagnose bleeds and to aid a road map for interventional radiologist for angiographic embolization. Colonoscopy might be necessary to exclude a lower GI bleed in case then patient presents with hematochezia. In case of obscure nature of bleed, and exclusion of upper and lower sources, a small bowel work up is necessary after stabilization. Wireless capsule endoscopy or small bowel spiral or balloon assisted enteroscopy will be necessary for further management in such situations. In rare situations, surgery could be contemplated and intra-operative small bowel enteroscopy might be necessary if all methods of endoscopy and angiographic embolization fail.

***Helicobacter pylori* treatment :**

A rapid urease test could be routinely performed during upper GI endoscopy in patients with peptic ulceration. However, in acute bleeds, it may be less accurate. Hence a subsequent urea breath test may be considered. *H. pylori* treatment is necessary of all eligible patients since it prevents recurrences and decreases the complication rates in case of recurrence. Patients who might be lifelong antiplatelets and long term NSAID usage should be eradicated for *H. pylori* if present. *H. pylori* treatment can be given a few weeks after recovery from bleeding episode since tolerance issues might be there.

Predictors of failure of endoscopic treatment

Hemodynamic instability

Significant comorbidity

> 4-6 U blood transfusion in 24 h

Endoscopic findings of the ulcer :

- Actively bleeding vessel Visible vessel
- Adherent clot
- Ulcer size > 2 cm

Indications for surgery in nonvariceal upper GI hemorrhage

Severe hemorrhage not responding to resuscitation

Recurrence of bleeding after initial control with endoscopic or medical measures

Second admission after treatment of ulcer hemorrhage

Prolonged bleeding with loss of 50% or more of blood volume

Blood transfusion > 4-6 U in 24 h

Age 60 or more with shock or anemia on admission

Certain endoscopic features of ulcer (ulcer size 2 cm, visible vessel underneath or on base of ulcer, active oozing or active arterial bleeding from the ulcer)

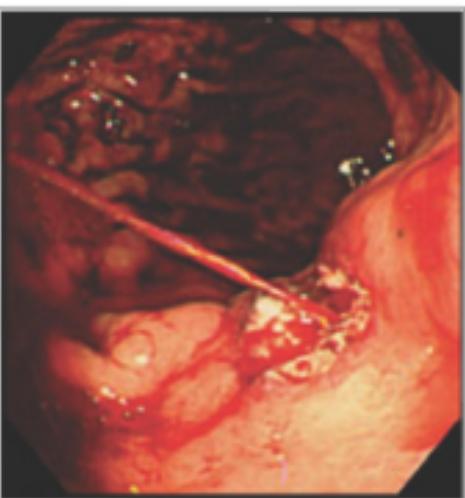
Maintenance proton pump inhibitor therapy :

Proton pump therapy needs to be continued for a few weeks or months depending upon the endoscopic findings. For duodenal ulcer without complications, 2 weeks of therapy with H. pylori eradication could be sufficient. For gastric ulcers without complications, 12 weeks of therapy with double dose along with H. pylori eradication is necessary. In all ulcer disease patients with complications like bleed, obstruction, they will need extended course of treatment until the

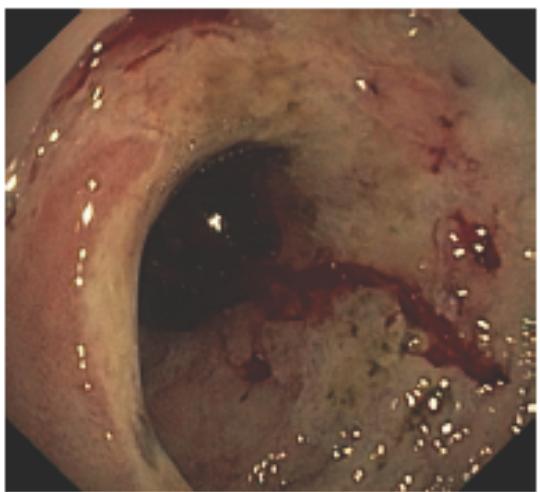
complication resolves and ulcers get eradicated endoscopically.

Rescue therapy for variceal bleeding :

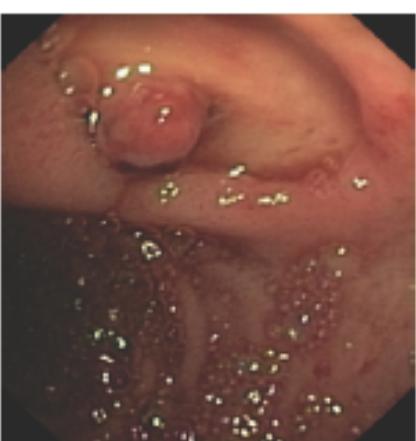
In patients who failed endoscopic therapy (10-20%) with banding for varices, or glue injection for gastric varices, Sengstaken Blackmore tube placement can be lifesaving rescue measure and work as a bridge until definitive therapy is initiated or performed therapy causes bleed control. Expected complications include aspiration, balloon



Forrester Class Ia



Forrester Class Ib



Forrester Class IIa



Forrester Class IIb



Forrester Class IIc



Forrester Class III

migration, esophageal necrosis due to pressure and perforation. Continuous esophageal balloon pressure measurement and intermittent deflation reduces the incidence of these complications.

Transjugular intrahepatic portosystemic shunt (TIPSS) is a very useful technique to control recurrent or refractory variceal bleeding, however, works as a bridge to transplant. Worsening of encephalopathy is a pertinent issue with this procedure which needs to be considered. Balloon occluded Transvenous Retrograde Obliteration of varices (BRTO) is another radiological intervention for treating bleeding fundal varices refractory to glue injection. This procedure doesn't have the risk of worsening encephalopathy since no shunt is created.

Self-expanding metal stents (SEMS) can be used for emergency bridging until the patient stabilizes since it is quick and rapid and may not need endoscopy also in some type of stents like Ella-Danis variety. They are effective in achieving hemostasis immediately, however after removal, they might be increased risk of rebleed if no definitive therapy is performed. Also cost of SEMS raises the expenditure limiting its usage routinely.

CONCLUSION

Acute upper GI bleeding is a common gastroenterological emergency with high mortality, particularly if variceal or in the elderly patient with comorbidities. Prompt clinical assessment, resuscitation and risk stratification using validated scoring systems like Rockall and Glasgow Blatchford scores are vital to ensure a positive outcome for the patient. Gastroenterologists along with critical care physicians should be informed early as should the surgical team. Where possible, blood should only be transfused if the Hb is <70g/L; however, each case should be carefully risk-assessed. Endoscopy within 24 h reduces rebleeding rates and need for surgery and is likely to reduce length of stay. Proton pump inhibitor therapy, vasoconstrictor therapy should be initiated as per the patient risk category. With expanded endoscopic armamentarium, endoscopists can treat bleeding

lesions more effectively, enabling adequate hemostasis in majority of patients. In situations where thermal or mechanical therapies fail at achieving hemostasis, sprayed hemostatic powder is a valuable rescue therapy to temporize severely bleeding lesions to allow time special treatment at later stage after stabilization. Ongoing or recurrent GI hemorrhage which fails to respond to endoscopic-medical management is an indication for urgent surgery. Radio-embolization is a growing useful adjunct in the available armamentarium for nonoperative management of upper GI bleeding. Although new endoscopic techniques and interventional radiology have decreased the role of surgery in management, the collaboration between the endoscopist and surgeon still remains pivotal.

REFERENCES

1. ASGE Standards of Practice Committee, Anderson MA, Ben-Menachem T, et al. Management of antithrombotic agents for endoscopic procedures. *Gastrointest Endosc* 2009; 70:1060.
2. Barkun AN, Almadi M, Kuipers EJ, et al. Management of Nonvariceal Upper Gastrointestinal Bleeding: Guideline Recommendations From the International Consensus Group. *Ann Intern Med* 2019; 171:805.
3. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet* 2000; 356:1318.
4. Carson JL, Guyatt G, Heddle NM, et al. Clinical Practice Guidelines From the AABB: Red Blood Cell Transfusion Thresholds and Storage. *JAMA* 2016; 316:2025.
5. Church NI, Dallal HJ, Masson J, et al. Validity of the Rockall scoring system after endoscopic therapy for bleeding peptic ulcer: a prospective cohort study. *Gastrointest Endosc* 2006; 63:606.
6. Corley DA, Stefan AM, Wolf M, et al. Early indicators of prognosis in upper

- gastrointestinal hemorrhage. Am J Gastroenterol 1998; 93:336.
7. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015; 47:a1.
 8. Hwang JH, Fisher DA, Ben-Menachem T, et al. The role of endoscopy in the management of acute non-variceal upper GI bleeding. GI Endo 2012; 75:1132.
 9. Laine L, Barkun AN, Saltzman JR, et al. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. Am J Gastroenterol 2021; 116:899.
 10. Lau JYW, Yu Y, Tang RSY, et al. Timing of Endoscopy for Acute Upper Gastrointestinal Bleeding. N Engl J Med 2020; 382:1299.
 11. Marmo R, Koch M, Cipolletta L, et al. Predicting mortality in non-variceal upper gastrointestinal bleeders: validation of the Italian PNED Score and Prospective Comparison with the Rockall Score. Am J Gastro 2010; 105:1284.
 12. Pang SH, Ching JY, Lau JY, et al. Comparing the Blatchford and pre-endoscopic Rockall score in predicting the need for endoscopic therapy in patients with upper GI hemorrhage. Gastrointest Endosc 2010; 71:1134.
 13. Weledji et al. Acute gastrointestinal bleeding: a review. International Journal of Surgery: Global Health (2020) 3:e18
 14. Wisam Jafar, Anisa Jabeen Nasir Jafar, Abhishek Sharma et al. Upper gastrointestinal haemorrhage: an update. Frontline Gastroenterology 2016;7:32–40. doi:10.1136/flgastro-2014-100492



Acute Coronary Syndrome - A Review

Dr. Pankaj Jariwala

Consultant Interventional Cardiologist
Yashoda Hospitals, Somajiguda, Hyderabad
docpjariwala@yahoo.co.in

Introduction

The acute coronary syndrome (ACS) is a collection of conditions characterized by a reduction in blood supply to the heart. ACS occurs as a result of plaque disruption in coronary arteries which is called atherosclerosis and is a symptom of CHD (coronary heart disease)(1). Heart tissue is damaged or destroyed by one of three forms of coronary artery disease that contribute to the acute coronary syndrome.

There are a variety of ACS types, including (**Figure -1**):

1. Angina that comes on suddenly and unexpectedly, even when you're at rest, is called **unstable angina**. When stable angina gets worse, it's a warning indication of an impending heart attack.
2. **NSTEMI** stands for "**non-ST-elevation myocardial infarction**," which is a type of heart attack that can be detected by blood tests along with an abnormal electrocardiogram (EKG).
3. **ST-elevation myocardial infarction (STEMI)** is a more severe form of heart attack that can be diagnosed by blood tests and an electrocardiogram (ECG). It happens when a major section of the heart goes without blood for an extended period (2).

Emergency department physicians, cardiologists, internists, pharmacists, and primary caregivers work together to treat ACS, which has high morbidity and mortality. The cardiologist is responsible for the treatment, while the primary care physician is responsible for prevention. It's

DIAGNOSTIC FLOW CHART

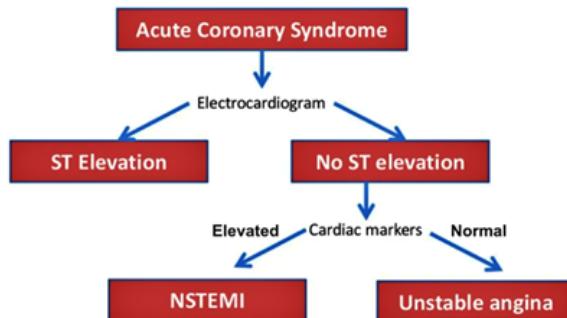


Figure 1: A flow chart for the diagnosis of acute coronary syndrome

important to stress the importance of quitting smoking, maintaining a good diet, getting regular exercise, and taking any necessary medications. Patients with severe diseases who do not comply with treatment have a poor prognosis while those who receive prompt care have a better chance of survival.

Risk factors and etiopathogenesis

Cigarette smoking, high blood pressure, type 2 diabetes, high cholesterol, being male, not getting enough exercise, having overweight, family history, and eating poorly are all major contributors to the disease. Vasospasm is another complication of cocaine addiction responsible for the ACS in younger individuals. Myocardial infarction occurs more frequently in people who have a family history of the condition before the age of 55.

The most important aspect of the pathophysiology of ACS is a decreased blood supply to a section of the cardiac muscle. This is typically brought on by the rupture of a plaque and the formation of a thrombus (**Figure -2**).

Vasospasm can occasionally be the root cause of ACS, regardless of whether or not atherosclerosis was present beforehand. As a consequence of this, the blood flow to a portion of the cardiac muscle is decreased, which leads to ischemia and, ultimately, infarction of that region of the heart.

Myocardial infarction with no obstructive coronary artery disease (MINOCA), which occurs in a minority of acute coronary syndrome cases and is more common in women than men, carries major diagnostic and therapeutic ambiguity(3).

An intimal rupture or less commonly vasa vasorum haemorrhage leading to the development of a false lumen in the arterial wall is considered to be spontaneous coronary artery dissection (SCAD) which is seen in < 5% cases of ACS (4).

Clinical features and examination

Substernal chest discomfort, which may be described as a crushing or pressure-like sensation, and which may radiate to the jaw and/or left arm is the hallmark symptom of ACS. This traditional presentation is not always present, and the initial symptom may be nonspecific and hard to detect. Common initial complaints include shortness of

breath, dizziness, headache, nausea, vomiting, epigastric discomfort, diaphoresis, and weakness. Patients with diabetes and those in their twilight years are more likely to experience ACS with nonspecific symptoms. In such situations, a great deal of scepticism is warranted (5).

Diaphoresis and generalized discomfort are common findings in a physical examination. A normal heart murmur is rather common. You can hear a gallop and a murmur every once in a while. Despite a normal physical examination, crackles in the lungs may be audible, suggesting congestive heart failure (CHF). The presence of oedema in both legs is a possible sign of congestive heart failure. Except in the presence of co-pathologies, the rest of the systems are usually within normal limits. When a patient presents with abdominal soreness on physical examination, the doctor should rule out more serious conditions including pancreatitis and gastritis. Aortic dissection should be considered if uneven pulses are present. When one leg swells more than the other, it's important to rule out a pulmonary embolism. Hence, it is crucial to do a complete physical examination to rule out any potentially fatal differentials.

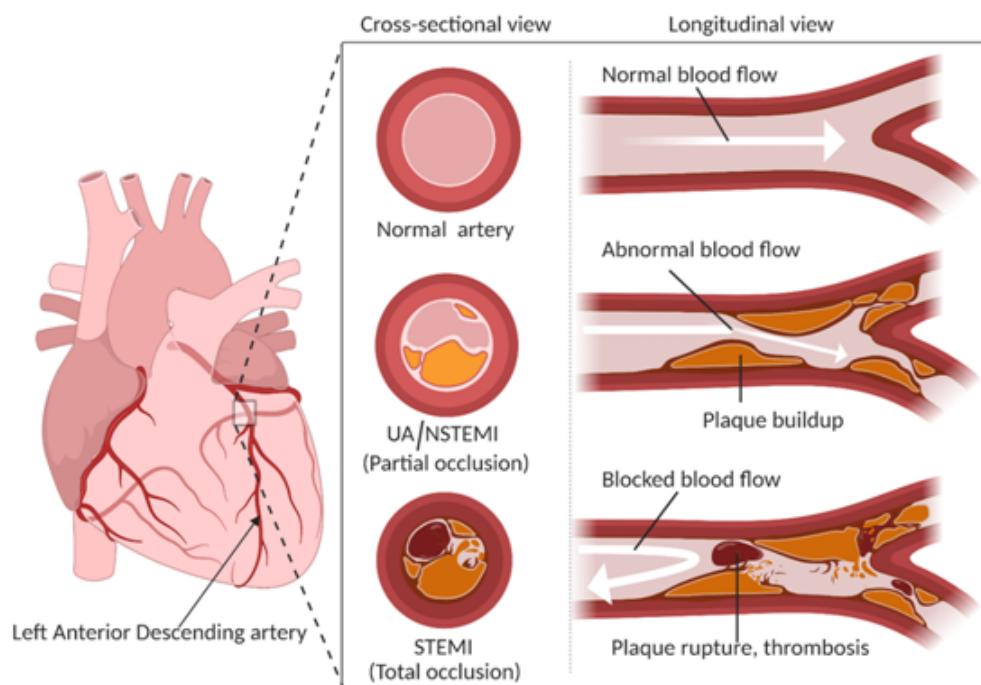


Figure 2: A schematic diagram depicting the etiopathogenesis of the acute coronary syndrome

Investigation

An electrocardiogram (ECG) is the primary tool for diagnosing unstable angina and can assist distinguish between STEMI and NSTEMI. According to recommendations from the American Heart Association (AHA), an ECG should be performed on any patient who presents with symptoms that raise suspicion of ACS as soon as possible upon arrival (**Figure 3**).

ECG changes in ACS

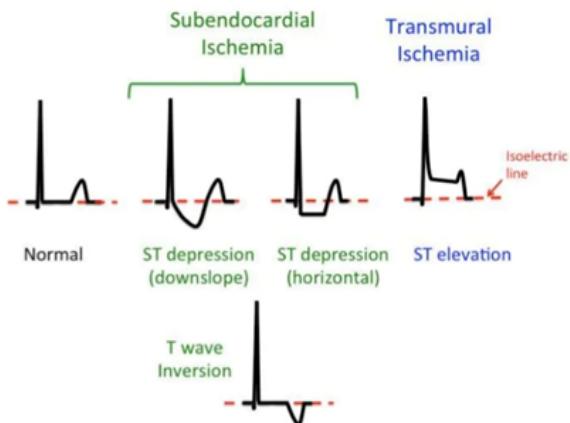


Figure 3: ECG changes in acute coronary syndrome

In a PCI centre, the cath lab should be engaged as soon as STEMI is confirmed. To differentiate between NSTEMI and myocardial ischemia without tissue loss, cardiac enzymes, especially troponin, CK-MB/CK ratio, must be measured. Chest x-rays help rule out heart attacks as a possible cause of chest pain by revealing other potential issues, such as pneumonia or pneumothorax. Similar to how a complete blood count (CBC), chemistry, liver function test (LFT), and lipase can distinguish between intraabdominal and extra-abdominal causes of chest pain, so too can a urinalysis. When appropriate, a thorough investigation into aortic dissection and pulmonary emboli should be conducted (6).

Management

If there are no contraindications, all ACS patients receive aspirin (300 mg) with heparin bolus and IV heparin infusion. Ticagrelor or clopidogrel antiplatelet treatment is advised(7). Local cardiologists decide. Thrombolysis patients do not receive ticagrelor. Morphine/fentanyl for pain and

oxygen for hypoxia are administered as needed (8). Sublingual or infusion nitroglycerine relieves pain. Nitroglycerine can produce severe hypotension in inferior wall ischemia and should be avoided. Arrhythmia monitoring should continue. STEMI/NSTEMI or unstable angina determines ACS treatment. STEMI patients should undergo urgent catheterization and percutaneous intervention (PCI) within 90 minutes (**Figure 4**), according to the AHA(9). If there is no PCI and the patient cannot be moved to the catheterization lab in 120 minutes, a thrombolytic such as tenectaplate is indicated. The AHA recommends a door-to-needle (TNK/thrombolytics) time of fewer than 30 minutes.



Figure 4: A patient presented with retrosternal chest pain and ecg demonstrated acute inferior wall stemi. Coronary angiography revealed thrombotic occlusion of the mid-segment of the right coronary artery. primary angioplasty using drug-eluting stent could establish the normal flowwith relief of the symptoms.

NSTEMI/Unstable Angina: Aspirin, heparin, and symptom management are considered. Urgent catheterization is advised if pain persists. If symptoms are well-controlled, catheterization and other evaluation methods such as myocardial perfusion testing can be scheduled depending on comorbidities. ACS requires admission and emergency cardiology. Depending on availability

and cardiologist choice, further workup may include CT angiography(1,2).

Unless contraindicated, all ACS patients should start beta-blockers, statins, and ACE inhibitors immediately. Depending on comorbidities and patient preference, non-PCI cases are treated with CABG or medically.

Conclusion

Coronary heart disease and acute coronary syndrome still kill the most people over 35. When assessing ACS patients, clinicians worldwide must be suspicious and vigilant. Community awareness and symptom identification are essential. Public education about lifestyle change and healthy living is another key to controlling this disease. Emergency medical services and skills are crucial to STEMI and ACS therapy. Lifestyle modification education—including smoking cessation, regular physical exercise, and dietary changes—is another important step in ACS control and prevention. This multi-pronged therapy controls this high-mortality condition.

References

1. Bhatt DL, Lopes RD, Harrington RA. Diagnosis and Treatment of Acute Coronary Syndromes: A Review. *JAMA* [Internet]. 2022 Feb 15 [cited 2022 Oct 28];327(7):662–75. Available from: <https://jamanetwork.com/journals/jama/fullarticle/2789023>
2. Bergmark BA, Mathenge N, Merlini PA, Lawrence-Wright MB, Giugliano RP. Acute coronary syndromes. Vol. 399, *The Lancet*. Elsevier B.V.; 2022. p. 1347–58.
3. Safdar B, Spatz ES, Dreyer RP, Beltrame JF, Lichtman JH, Spertus JA, et al. Presentation, Clinical Profile, and Prognosis of Young Patients With Myocardial Infarction With Nonobstructive Coronary Arteries (MINOCA): Results From the VIRGO Study. *J Am Heart Assoc* [Internet]. 2018 Jul 1 [cited 2022 Oct 28];7(13). Available from: <https://pubmed.ncbi.nlm.nih.gov/29954744/>
4. Nishiguchi T, Tanaka A, Ozaki Y, Taruya A, Fukuda S, Taguchi H, et al. Prevalence of spontaneous coronary artery dissection in patients with the acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care* [Internet]. 2016 Jun 1 [cited 2022 Oct 28];5(3):263–70. Available from: <https://pubmed.ncbi.nlm.nih.gov/24585938/>
5. Gilutz H, Shindel S, Shoham-Vardi I. Adherence to NSTEMI Guidelines in the Emergency Department: Regression to Reality. *Crit Pathw Cardiol* [Internet]. 2019 Mar 1 [cited 2022 Oct 28];18(1):40–6. Available from: <https://pubmed.ncbi.nlm.nih.gov/30747764/>
6. Campanile A, Castellani C, Santucci A, Annunziata R, Tutarini C, Reccia MR, et al. Predictors of in-hospital and long-term mortality in unselected patients admitted to a modern coronary care unit. *J Cardiovasc Med (Hagerstown)* [Internet]. 2019 May 1 [cited 2022 Oct 28];20(5):327–34. Available from: <https://pubmed.ncbi.nlm.nih.gov/30865139/>
7. Chen WWC, Law KK, Li SK, Chan WCK, Cheong A, Fong PC, et al. Extended dual antiplatelet therapy for Asian patients with acute coronary syndrome: expert recommendations. *Intern Med J* [Internet]. 2019 Mar 1 [cited 2022 Oct 28];49 Suppl 1:5–8. Available from: <https://pubmed.ncbi.nlm.nih.gov/30815979/>
8. Duarte GS, Nunes-Ferreira A, Rodrigues FB, Pinto FJ, Ferreira JJ, Costa J, et al. Morphine in acute coronary syndrome: systematic review and meta-analysis. *BMJ Open* [Internet]. 2019 Mar 1 [cited 2022 Oct 28];9(3). Available from: <https://pubmed.ncbi.nlm.nih.gov/30878985/>
9. Kerneis M, Nafee T, Yee MK, Kazmi HA, Datta S, Zeitouni M, et al. Most Promising Therapies in Interventional Cardiology. *Curr Cardiol Rep* [Internet]. 2019 Apr 1 [cited 2022 Oct 28];21(4). Available from: <https://pubmed.ncbi.nlm.nih.gov/30868280/>



Organophosphorus poisoning-focus on management aspects

Dr Raviraja V Acharya

Professor and Head, Department of Medicine, KMC Manipal

Dr Siddharth Gosavi

Senior resident, Department of Medicine, KMC Manipal

Dr Gokul Krishnan V.S

Department of Medicine, KMC Manipal

Introduction

Organophosphorus compounds are cholinesterase inhibitors used extensively in domestic and industrial life. They are used as insecticides, herbicides, industrial chemicals etc. Carbamates has similar mechanism of action and similar treatment protocol is to be followed. Organophosphorus compounds are extensively used in domestic and industrial life. Common exposures occur in household, occupational, military, intention of self-harm, unintentional

Epidemiology

Approximately 300,000 fatalities have been noted globally with exposure of three million individuals to organophosphate compounds. A study from India noted that over 40% cases of poisoning was secondary to organophosphate compounds.

Risk factors

Organophosphorus poisoning can be accidental or intentional. Route of exposures known are inhalational, oral and cutaneous. Occupation at highest risk of accidental exposure is those

involved in agricultural activities and rarely healthcare workers if adequate measures are not taken during management of cases of cutaneous exposure.

Intentional self-harm by oral consumption of organophosphorus compound is also most common among the farmers due to wide availability of the compound. Those with underlying illness like depression are particularly at greater risk.

MECHANISM OF ACTION

Organophosphorus compounds are substances containing carbon and phosphorous acid. Skin, lungs and gastrointestinal tract are the main organs which are involved in the absorption of organophosphorus compounds. They inhibit the enzyme acetylcholinesterase enzyme by binding to it. Due to this, there is an excess of acetylcholine at the neuromuscular junction and the neuronal synapse. This acetylcholinesterase-organophosphorus compound undergoes conformation which makes the enzyme irreversibly resistant to reactivation by oximes.

Use	Organophosphorus compound	Brand name
Insecticide	Malathion, parathion, fenthion, chlorpyriphos, profenofos	Mal-50, Profex, Profen
Herbicide	Tribufos, merphos, Glyphosate	Roundup
Antihelminthic	Trichlorfon	Trichlorfon
Ophthalmic agents	Echothiophate, Isoflurophate	
Industrial chemical	tricresylphosphate	
Nerve gas	Sarin, soman, tabun	

Clinical features

Timing of onset of clinical features post exposure depends on dose and route of exposure with early manifestations seen following oral and inhalational route as compared to dermal exposure. Clinical manifestations can be delayed upto twelve hours following dermal exposure. Lipophilic compounds shows delayed onset and prolonged illness due to rapid uptake by adipose tissue and slow redistribution from tissue.

Features seen are secondary to excess acetylcholine acting at muscarinic and nicotinic receptors. Cardiac features seen are bradycardia and high blood pressure. In severe cases, conduction defects and myocardial ischemia are noted. Large volume consumption may cause resistant hypotension possibly due to myocardial dysfunction or peripheral vasodilation by direct action of poison.

Acute neurological manifestations are miosis, fasciculations and weakness.

Certain cases develop intermediate syndrome one to four days following acute episode and is noted by proximal muscle weakness including neck weakness. Higher mental function is also affected in form of agitation, confusion and seizures. This is often confused for atropine toxicity. A rare delayed neurological complication of organophosphorus poisoning is OPIDN (organophosphorus induced delayed neuropathy). This entity occurs after three weeks and results in predominant motor deficit affecting extremities which may progress proximally. Paraesthesiae are also commonly noted.

Respiratory features are bronchospasm and profuse secretions. In addition to the above factors, respiratory insufficiency can occur secondary to aspiration, respiratory muscle weakness and central respiratory centre depression. Hypersalivation, emesis and diarrhoea are the gastrointestinal manifestations. Other systemic manifestations are hyper lacrimation and micturition. Occasionally acute kidney injury can occur, either secondary to direct toxicity by compound or due to systemic complications like

hypotension or sepsis. It may be severe enough requiring renal replacement therapy.

It is to be noted that cases can present with atypical presentation in the following scenarios

- Has received treatment
- Consumption of other substances (commonest is alcohol)
- Mydriasis and tachycardia can occur due to stimulation of nicotinic receptors in sympathetic ganglia
- Lipophilic compounds can result in delayed onset and prolonged illness due to reasons mentioned above

Differential diagnosis

There are other conditions that can present with symptoms of organophosphorus poisoning

Toxicity of carbachol which is a muscarinic receptor agonist, poison hemlock and mushroom (*inocybe,clitocybe*) can present with features of OP poisoning.

Opioid withdrawal cases present with agitation, lacrimation and rhinorrhea. Unlike organophosphorus poisoning, opioid withdrawal results in pupillary dilation.

Medical conditions like acute autonomic neuropathy though rare entity can mimic organophosphorus poisoning. Acute attacks of pheochromocytoma, systemic mastocytosis and carcinoid syndrome can have features of acute organophosphorus poisoning. Systemic mastocytosis, carcinoid syndrome and pheochromocytoma results in tachycardia in contrast to bradycardia of organophosphorus poisoning.. During attacks of systemic mastocytosis patient is usually hypotensive.

DIAGNOSIS

Measurements of RBC acetylcholinesterase and plasma cholinesterase (pseudo cholinesterase) are the blood markers which are used for the diagnosis. Plasma cholinesterase is more

commonly used as it is easily available even though RBC acetylcholinesterase accurately reflects nervous system OP acetylcholinesterase inhibition. The normal serum pseudo cholinesterase is 5320-12920 U/L for men and 4260-11250 U/L for women. However, it is important to note that plasma cholinesterase may not correlate with severity of the condition and cannot be used for prognosis and guiding in treatment. Normalisation of level takes long time (6-12 weeks) compared to rapid recovery at tissue level. Other non-specific lab findings are leucocytosis, hemoconcentration, metabolic acidosis, hyperglycemia, hypokalemia, hypomagnesemia, increased troponin levels, increased amylase levels and deranged liver function tests. ECG can show prolonged QTc interval and sinus tachycardia. ABG may reveal hypoxemia.

MANAGEMENT

Patients with poor GCS have to undergo endotracheal intubation and mechanical ventilation. Patients who have consumed organophosphorus poison are at an increased risk of respiratory arrest due to CNS respiratory centre depression, nicotine receptor induced diaphragmatic and respiratory muscle weakness, bronchoconstriction and excessive secretions. Volume status and hydration has to be maintained with crystalloids. On atropine patients are kept nil per oral for days to weeks better administer dextrose containing fluids.

Pralidoxime and atropine are the mainstays of treatment of organophosphorus compound poisoning.

Atropine-2mg is administered IM as first dose. After first dose, if patient still has symptoms, patient should be given 4mg additional dose. Still if a patient is unconscious or has severe symptoms, 6mg should be administered in rapid succession. Improvement has to be reassessed after every 10-15 minutes. Atropine dose should be doubled every 5 minutes. Atropine infusion has to be started which should consist of 10-20% of total dose required for atropinization. Pupils, heart rate and secretions have to be continuously reassessed.

The therapeutic target is cessation of respiratory secretions and bronchospasm. Tachycardia and mydriasis should not be used for monitoring improvement as they can exist due to hypoxia, hypovolemia and sympathetic activity. Patients may need atropine infusion for several days. Atropine infusion should be titrated closely to keep patient fully atropinised for first few days then gradually tapered. (As body metabolises / excretes poison need for atropine gradually comes down) There is no fixed dose of atropine. Never to stop atropine infusion abruptly.

Pralidoxime- Pralidoxime is a cholinesterase reactivating agent that is effective in treating both muscarinic and nicotinic symptoms. Pralidoxime is administered IV at dose of 30 mg/kg body weight IV over 30 minutes and can be repeated after 1 hour if necessary. Following this, the same dose can be repeated 12th hourly as required for upto three days. Improvement in muscle strength and reduction in fasciculations can be used for monitoring efficacy of oxime and deciding on further dosage. The main aim of oximes is to prevent intermediate syndrome and organophosphorus induced delayed neuropathy. Oximes are beneficial when used in the first 3 days of illness as they act competitively with poison on cholinesterase receptor. Oximes are not recommended in carbamate poisoning.

While administering oxime, ensure that patient is under cover atropine. This is to prevent paradoxical worsening secondary to transient oxime induced cholinesterase inhibition.

Any seizure in organophosphorus poisoning patients should be treated with a benzodiazepine like diazepam. It decreases neurocognitive decline.

In extremely agitated patients, we must try to find out if it is secondary to poison itself or atropine toxicity (more likely). Pupils and secretion status can be assessed to look at level of atropinisation. If well atropinised we may come down on atropine and substitute with glycopyrrolate as required for secretions. If not atropinised, it is prudent to continue atropine while attributing the restless state to organophosphorus compound. Hypoxia,

electrolyte imbalance, thiamine deficiency and alcohol withdrawal to be looked for and treated.

Decontamination-Decontamination should be performed by removing the patient's clothes and aggressive irrigation of the affected areas especially in topical exposure. Gastric lavage can be performed but there is high risk of aspiration pneumonia in patients with poor GCS and excessive secretions. Activated charcoal (adsorbent) should be given to the patients within 1 hour of ingestion at a dose of 1g per kg. It is not given when time of ingestion has crossed 1 hour.

Supportive care

Oxygen, ventilation, insertion of Foley's catheter before start of atropine, back care, dextrose containing IV fluids with thiamine, adequate parenteral hydration, recognition of infection and suitable antibiotics and close monitoring and management in calm ICU or HDU are essential for better outcome. Suitable restrain is essential initially when atropinised.

As atropine causes decreased gastric emptying and intestinal motility, patient need to be on only IV fluids while on atropine. Oral or RT feeding is not advised for fear of aspiration, distension of abdomen further compromising ventilation. On average patients requires 3-7 days of atropine and in an otherwise healthy person 2.0-2.5 litres of dextrose containing fluids with thiamine give just enough calories to prevent ketosis. It is important to audit and down titrate dose of atropine periodically and stop at the earliest. If need for atropine goes beyond 7 days better to consider total parenteral nutrition. Resuming oral / RT feeding while on atropine practised by some may be potentially harmful and should be discouraged.

Complications

Respiratory failure, neuromuscular weakness, hemodynamic collapse (hypotension), respiratory infection, sepsis, coma and acute kidney injury are common or important complications encountered while managing OP poisoning cases. Severe hypotension, coma and progressive kidney injury carry bad prognosis.

Prevention

Availability of OP should be restricted, users to be educated on safe keeping, proper labelling of containers, not to keep poison in unlabelled containers similar to water or juice bottles. Also about suitable dilution requirement of given preparation, personal protection while spraying the poison in the fields (gloves, mask, non-porous body gown). Possibility of Inhalation and cutaneous exposure while using to be highlighted to end users. Utmost care to be taken by healthcare personnel with respect to personal protective equipment (gloves, gown and mask) especially while handling cases.

In cases of intentional self-harm, a psychiatry consultation and detailed evaluation to be obtained ideally in the same admission once patient has recovered from poisoning, as an essential secondary prevention method.

Plan for discharge

Prior to discharge it must be ensured that patient has overcome acute crisis as well as intermediate syndrome. If a patient has recovered from acute complication and has not developed intermediate syndrome, assess the risk of development of intermediate syndrome prior to discharging. Risk factors include lipophilic compound and inadequate use of oximes. To counsel patient regarding possible delayed complications like OPIDN (organophosphorus induced delayed neuropathy) where they may develop new onset progressive weakness and paraesthesia upto three weeks following acute episode.

References

1. Eddleston M, Phillips MR. Self poisoning with pesticides. BMJ 2004; 328:42.
2. Nadeem, M.N., Maqdoom, M. and Akif, M.E. (2020) A prospective observational study on pattern of poisoning cases reported to emergency department of a teaching hospital in South India, *Biomedical and Pharmacology Journal*, 13(4), pp. 1863–1869.

3. Eyer P. The role of oximes in the management of organophosphorus pesticide poisoning. *Toxicol Rev* 2003; 22:165.
4. Sidell FR. Soman and sarin: clinical manifestations and treatment of accidental poisoning by organophosphates. *Clin Toxicol* 1974; 7:1.
5. Groszek B, Pach J, K³ys M. Intermediate syndrome in acute fenitrothion poisoning. *Przegl Lek* 1995; 52:271.
6. Dickoff DJ, Gerber O, Turovsky Z. Delayed neurotoxicity after ingestion of carbamate pesticide. *Neurology* 1987; 37:1229.
7. Abou-Donia MB. Organophosphorus ester-induced chronic neurotoxicity. *Arch Environ Health* 2003; 58:484.
8. Aygun D, Onar MK, Altintop BL. The clinical and electrophysiological features of a delayed polyneuropathy developing subsequently after acute organophosphate poisoning and its correlation with the serum acetylcholinesterase. *Electromyogr Clin Neurophysiol* 2003; 43:421.



Acute Ischemic Stroke

Dr C.J. Selvakumar MD DM

Senior Assistant Professor

Dr Sanjo K John MD DNB

(Junior Resident), Department of Neurology,
Coimbatore Medical College.

Introduction

Stroke is a serious neurological disease and constitutes a major cause of death and disability throughout the world. The pathophysiology of stroke is complex and involves excitotoxicity mechanism, inflammatory pathways, oxidative damage, ionic imbalances, apoptosis, angiogenesis and neuroprotection. The ultimate result of ischemic cascade initiated by acute stroke is neuronal death along with an irreversible loss of neuronal function. Therapeutic strategies in stroke have been developed with two main aims: restoration of cerebral blood flow and the minimization of the deleterious effect of ischemia on neurons. Intense research spanning over the last two decades has witnessed significant therapeutic advances in the form of carotid endarterectomy, thrombolytics, anticoagulant therapy anti platelet agents and neuroprotective agents and treating associated risk factors such as hypertension and hyperlipidemia. Till date only one FDA approved drug is available for ischemic stroke that is the serum protease tissue type plasminogen activator, utility of which is limited by short therapeutic window.

RISK FACTORS

Risk factors of ischemic stroke are classified as modifiable and non modifiable risk factors. Non modifiable risk factors include old age, male gender, ethnicity, family history and prior history of stroke. Modifiable risk factors again classified into behaviour and -lack of physical activity, tobacco use, alcohol abuse and illicit drug use and non behavioral factors including socio-economic status, arterial hypertension, dyslipidemia, heart disease and carotid artery disease. Potentially

modifiable risk factors include diabetes mellitus, hyperhomocysteinemia and left ventricular hypertrophy. Less well documented risk factors include blood markers C reactive protein, ankle brachial blood pressure ratio, silent cerebral infarct, white matter hyperintensities on MRI and degree of carotid artery intima media thickness.

PATHOPHYSIOLOGY OF CEREBRAL ISCHEMIA

A cascade of complex biochemical events occurs seconds to minutes after cerebral ischemia. Cerebral ischemia is caused by reduced oxygen delivery to the microcirculation. Ischemia causes impairment of brain energy metabolism, loss of aerobic glycolysis, intracellular accumulation of sodium and calcium ions, release of excitotoxic neurotransmitters, lactate elevation with local acidosis, free radical production, swelling of cell, over activation of lipases and proteases and cell death.

Many neurons undergo apoptosis after brain ischemia. Ischemic brain injury is exacerbated by leukocyte infiltration and development of brain edema. These biochemical changes have been the targets for many strategies aimed at neuroprotection.

Clinical features:

A number of syndrome results from ischemia involving the central nervous system. It can be carotid artery system syndrome- acute infarct in the middle cerebral artery territory, syndrome of anterior cerebral artery and related blood vessels, vertebrobasilar system stroke, lacunar infarction, syndrome of thalamic infarction and watershed ischemic syndrome. Acute infarct in the MCA territory presents with hemiplegia, aphasia and

facial palsy while posterior circulation stroke predominantly presents with ataxia, nystagmus and nasal regurgitation.

Diagnosis and Management:

Rapid diagnosis of stroke and initiation of treatment are important to maximize recovery, prevent recurrent stroke and prevent complications. Patient with a TIA or an acute stroke regardless of security, presenting within 72 hours of symptom onset should be admitted to the hospital for emergency evaluation and treatment preferably in a stroke unit or Intensive Care Unit. Emergency care involves attention to the protection of the airway to avoid obstruction, hypoventilation and aspiration.

Pulse oximetry or arterial blood gases may be indicated. Supplemental oxygen and ventilatory assistance should be added if needed. Mild hypothermia prevents brain function from ischemic injury. BP should be maintained and proper blood circulation should be maintained. Optimal arterial blood pressure post stroke appears to range 160 - 200 mmHg for systolic pressure and 70- 110 mmHg for diastolic blood pressure. American heart Association guidelines suggests the lowering arterial blood pressure immediately post stroke only if the patients blood pressure is above 220/130 mmHg unless the patient is a candidate for thrombolytic therapy in which target goal of less than 185 /110 mmHg is appropriate prior to thrombolysis.

Immediately after the patient arrival in the emergency room, blood should be sent for appropriate studies, including a complete blood cell count, PT ,INR APTT and a general chemistry screen. A focused neurological examination should be performed to assess the neurological stability and determine the extent of infarction. General signs that point towards a large infarction are forced eye deviation, hemiplegia and altered consciousness . An NIHSS value of greater than 15 is another general indicator of a large infarction. Once stability of airway breathing and circulation is determined and a focused neurological examination is performed, the patient should be

sent immediately for emergency brain imaging with cranial CT Scan without contrast and MRI diffusion imaging. This can point a way to treat the patient with TPA or to avoid antithrombotics in patients with intracranial bleed.

The three main principles of acute stroke care are

1. Achieve timely recanalization of the occluded artery and reperfusion of the ischemic tissue.
2. Optimise collateral flow.
3. Avoid secondary brain injury.

chemical thrombolysis with recombinant tissue plasminogen activator also known as alteplase and mechanical thrombectomy with a retrievable stent are the two evidence-based strategies to achieve reperfusion.

IV Thrombolysis

The first landmark clinical trial that demonstrated the safety and efficacy of IV-tPA in 1995 transitioned the treatment for AIS from being purely symptomatic to a highly time-sensitive matter. It shows that if IV-tPA is administered within the first 3 hours of symptom onset, patients are at least 30% more likely to have only minimal or no disability on the 90-day mark. Based on the European study Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke (ECASS-3), the American Heart Association/ American Stroke Association (AHA/ASA) extended the IV-tPA window from 3 to 4.5 hours in 2009 with additional exclusion criteria.Dose of alteplase (0.9 mg/kg (not to exceed 90 mg total dose), with 10% of the total dose administered as an initial intravenous bolus over 1 minute and the remainder infused over 60 minutes.)

Tenecteplase(the preferred dose is 0.25 mg/kg (maximum 25 mg).), a newer thrombolytic agent with high fibrinogen specificity and long half-life, allowing it to be given as a single bolus, had promising results in recent clinical trials.

Endovascular Therapy

Multiple trials have shown the efficacy of EVT in

addition to standard medical care in improving the overall outcome of AIS patients with proximal MCA or internal carotid artery (ICA) occlusion when EVT was performed within either 6 hours, 8 hours, or 12 hours of symptom onset. Two recent clinical trials showed that the time window can further be extended to 24 hours postsymptom onset if there is either mismatch between the clinical deficit and the infarct size or perfusion mismatch on imaging.

Rehabilitation

Early mobilization is thought to be of great importance in order to maximize functional recovery and independence after AIS.

Nutrition.

As in the case with all critically ill neurologic patients, enteral feeding should be started within 48 hours to avoid protein catabolism and malnutrition. A small-bore nasoduodenal feeding tube may reduce the risk of aspiration events. Assessment of speech and swallowing function is imperative in AIS patients to determine the need for long-term enteral nutrition with percutaneous enteric gastrostomy.

Risk Factor Modification (Secondary Prevention)

Classification of AIS subtype/etiology is based on the definitions used in the multicenter Trial of Org 10172 in Acute Stroke Treatment and include the following:

- 1) large-artery atherosclerosis, 2) cardioembolism, 3) small-vessel occlusion, 4) stroke of other determined etiology, and 5) stroke of

undetermined etiology (cryptogenic). A thorough workup consisting of vascular imaging, MRI, transthoracic echocardiogram with bubble assessment (for shunt evaluation), lipid panel, and hemoglobin A1C, among others, is required to determine the underlying etiology and tailor the appropriate secondary stroke prevention. Antiplatelet therapy is an important cornerstone of treatment for the prevention of stroke and transient ischemic attacks (TIAs). Aspirin is the most commonly used agent, since it is relatively safe, cheap, and widely available. The Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack (CHANCE) trial, a study with primary Asian ethnicity, demonstrated a reduction of 90-day stroke incidence after minor strokes (NIHSS < 4) or TIAs with the combination therapy aspirin and clopidogrel (dual antiplatelet therapy) for 21 days poststroke when compared with aspirin alone, without demonstrating an increase in hemorrhages.

Statins are the drug of choice for dyslipidemia, which is an important risk factor for atherosclerotic disease. In recent years, studies showed that statins have a pleiotropic effect beyond lowering cholesterol including being antithrombotic, antiinflammatory, and endothelial protective effect.

CONCLUSIONS

Over the last few decades, multiple new innovations have introduced a new era of vascular neurology and included more patients for acute treatment, leading to improved outcome. Despite these groundbreaking changes, the constant decline in stroke mortality has slowed down.



Anaphylaxis

Dr. Vajrapu Rajendra

Head, Department of Critical Care
Aware Gleneagles Global Hospitals, Hyderabad
rvajrapu@gmail.com

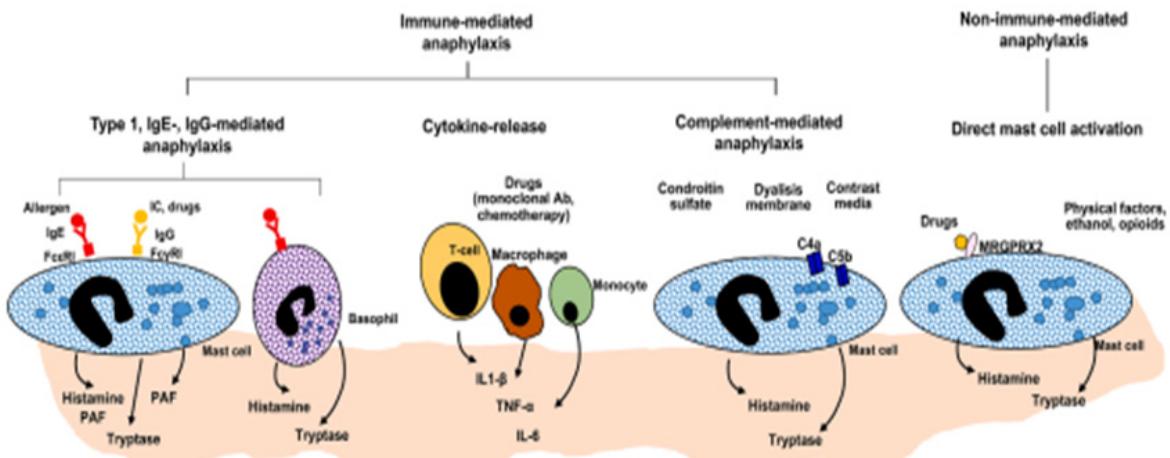
Anaphylaxis is an acute, fatal hypersensitivity disorder, defined as a generalized, rapidly evolving, multi-systemic allergic reaction. Without treatment, anaphylaxis is often lethal due to its rapid progression to respiratory collapse. Anaphylactic reactions are classified as IgE-mediated responses, while anaphylactoid reactions as IgE-independent events. Presently both the terms are consolidated to the unidiagnosis of anaphylaxis , as the treatment goals are same.

Despite its increasing frequency and morbidity, it remains often underdiagnosed and improperly managed. Lifetime prevalence was estimated to range from 0.05–5.1%. Recurrence rate is also a matter of concern, being present in 26.5–54.0% of the cases. In a multicenter study in the USA, only 24% of those with severe allergic reactions received epinephrine at the ED, and only 16% of those patients were given self-injectable epinephrine. In another study in Australia, the use of adrenaline was just under 40% in ED.

Pathophysiology

Anaphylaxis typically occurs within minutes to hours after exposure to an allergen. Signs and symptoms commonly appear in the mucosal, respiratory, cardiovascular, neurologic and gastrointestinal system. The most common triggers of anaphylaxis are food, insect venom, and medication.

immunoglobulin (Ig)-E-mediated anaphylaxis has been characterized by the acute degranulation of mast cells and basophils after release of pre-formed mediators, such as tryptase, histamine and platelet activating factor (PAF), mediators, such as leukotrienes, prostaglandins ,cytokines and interleukins. These products determine the constellation of the anaphylactic signs and symptoms . The inflammatory response is then mediated by TNF-alpha (tumor necrosis factor), both as a preformed and late-phase reactant.



The detailed physiology of these chemical mediators is as follows:

- Histamine increases vascular permeability and vasodilation leading to hypoperfusion of tissues. The body responds to these changes by increasing heart rate and cardiac contraction.
- Prostaglandin D functions as a bronchoconstrictor, with simultaneous cardiac and pulmonary vascular constriction. It also potentiates peripheral vasodilation thus contributing to the hypo-perfusion of vital organs.
- Leukotrienes add to bronchoconstriction, vascular permeability, and induce airway remodeling.
- The platelet activation factor also acts as a bronchoconstrictor and increases vascular permeability.
- TNF-alpha activates neutrophils (as part of stress response leukocytosis) and increases chemokine synthesis.

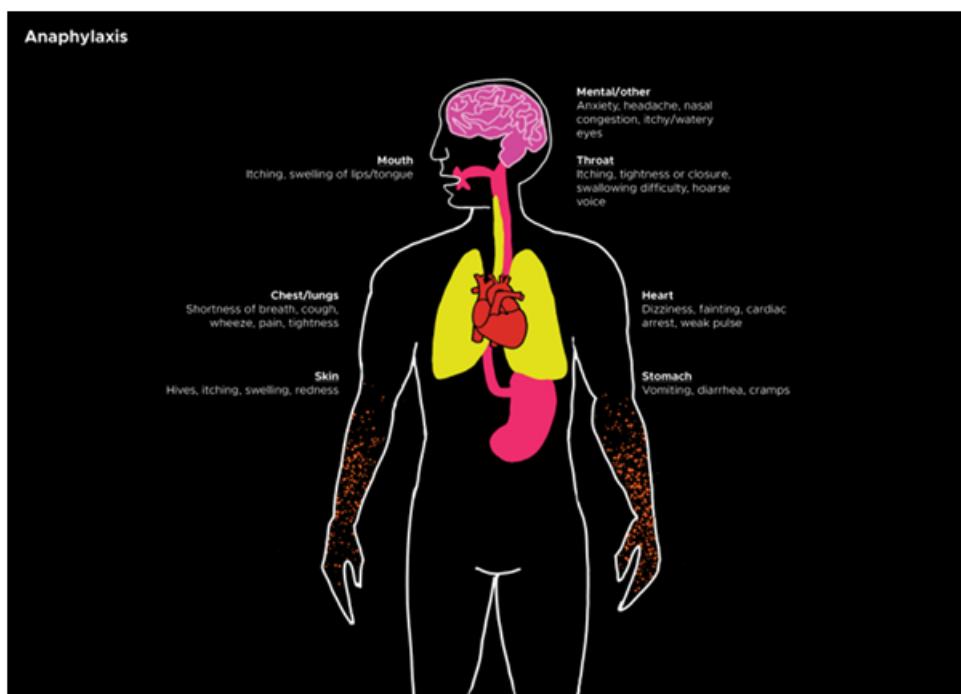
Clinical presentation

It often begins as a mild allergic reaction. The primary symptoms depend on the mode of

exposure to the causative antigen. While cutaneous flushing with pruritus and urticaria are common, they may not develop until after respiratory symptoms occur, which is common in oral exposures. Fullness or a "lump in the throat," persistent clearing of the throat, or difficulty breathing are all concerning symptoms of anaphylaxis and should be treated aggressively. Other respiratory symptoms include hoarseness, wheezing, and stridor. Gastrointestinal (GI) symptoms are present in 25% to 30% of patients. Signs of end-organ damage from hypo-perfusion include abdominal pain and cramps, vomiting, hypotonia, syncope, or incontinence.

Around 50% of the anaphylactic-related causalities happen within this first hour, hence the first hour after the first symptom is the critical for treatment. It is important to note that the more rapid the onset and progression of symptoms, the more severe the disease process. Morbidity and mortality are most often related to loss of airway and distributive shock. Early recognition and aggressive treatment greatly reduce the risk of adverse outcomes.

The first hour is not the only time of concern; however, as anaphylactic reactions can also present in a biphasic manner in up to 20% of cases. Even after successful management of the initial



presenting symptoms, there can be a recurrence of symptoms peaking 8 to 11 hours after the initial reaction.

There are four recognised patterns of anaphylaxis.

- 1. Uniphasic :** the most common type, with an estimate of 84-94% It usually peaks within hours after the symptom then resolves on its own or with treatment within several hours.
- 2. Protracted :** can last for hours or days without resolving any symptoms.
- 3. Refractory:** persistence of anaphylactic symptoms despite appropriate dosing and symptom management, as well as reactions that occur after at least three doses of epinephrine administration
- 4. Biphasic :** clinically significant in 4% to 5% of patients with diagnosed anaphylaxis. The time gap between the absence and reoccurrence of symptoms may range from 1 hr to 48 hrs

Triggers

A variety of drugs, ranging from antibiotics to analgesics, can cause anaphylaxis.

NSAIDS

It is also caused by cross reactivity in some patients who are not IgE dependent, with the most

commonly encountered drugs being diclofenac, propionic acid derivatives, and ibuprofen.

Beta Lactum antibiotics

Beta lactums are the second most common cause of anaphylaxis, after amoxicillin, and there is an increased prevalence of clavulanic acid causing allergy.

Radio contrast media(RCM): RCM related anaphylaxis has come down significantly after the introduction of non-ionic low molecular compounds. Although there is a slight risk of patients having an anaphylactic attack in patients on non-ionic contrast , it accounts for 27% of the fatal drug-induced anaphylaxis cases.

The diagnosis of anaphylaxis is a clinical diagnosis; thus, laboratory studies or other diagnostics are not necessary. Most anaphylactic deaths occur within the first hour after antigen exposure, rapid recognition and action are imperative. Laboratory testing is usually ineffective in patients experiencing an anaphylactic reaction, but serum tryptase levels are sometimes used as a marker because they are elevated in several hours.

Mimickers of anaphylaxis include acute exacerbation of asthma, vocal cord dysfunction, angioedema, epiglottitis, vasovagal syncope, acute anxiety, panic attack, carcinoid syndrome and septic shock. A normal tryptase level does not exclude anaphylaxis

Anaphylaxis is highly likely when any one of the following three criteria are fulfilled

1. Acute onset of an illness (minutes to several hours) with involvement of the skin and/or mucosal tissue (e.g., generalized hives, pruritus or flushing, swelling of the lip, tongue, or uvula) and at least one of the following
 - a. Respiratory compromise (e.g., hoarseness, cough, chest tightness, dyspnea, wheeze-bronchospasm, stridor, cyanosis, reduced PEF, hypoxemia)
 - b. Reduced BP or associated symptoms of end-organ dysfunction [e.g., hypotonia (collapse), syncope, incontinence]
2. Two or more of the following that occur rapidly (minutes to several hours) after exposure to a likely allergen
 - a. Involvement of the skin-mucosal tissue (e.g., generalized hives, pruritus or flushing, swelling of the lip, tongue, or uvula)
 - b. Respiratory compromise (e.g., hoarseness, cough, chest tightness, dyspnea, wheeze-bronchospasm, stridor, cyanosis, reduced PEF, hypoxemia)
 - c. Reduced BP or associated symptoms (e.g., hypotonia [collapse], syncope, incontinence)
 - d. Persistent gastrointestinal symptoms (e.g., abdominal cramps, vomiting)
4. Reduced BP after exposure to a known allergen (within minutes to several hours)
 - a. Infants and children: low systolic BP (age specific) or >30% decrease in systolic BP^b
 - b. Adults: systolic BP of <90 mmHg or >30% decrease from a baseline measurement

BP, blood pressure; PEF, peak expiratory flow.

^aAdapted from diagnostic criteria proposed by American National Institute of Allergy and Infectious Diseases and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) [(Sampson et al., 2006)].

^bLow systolic blood pressure in children is defined by age: 1 month to 1 year: < 70 mmHg; age 1-10 years: < [70 mmHg + (2 × age)]; age 11-17 years: < 90 mmHg.

Initiate evaluation and management

It has been seen that the time from anaphylaxis to cardiac arrest was 30 min for food, 15 min for venom, and 5 min for medications . It is always important to identify high-risk patients—those who are allergic to peanut or tree nuts, patients on beta blocker drugs ,elderly.

If a person is suspected to have anaphylaxis, inform the person, people nearby, or caregivers that an emergency call should be made immediately, or the patient should be transported directly to an emergency department for care by medical workers. While waiting for emergency medical technicians, the suspected allergen should be removed if possible. People should be placed on the back, or should be sitting up if there is respiratory distress. If vomiting occurs, ensure that the head is turned slightly downward and any substance in the airway should be cleared away to prevent aspiration. If an epinephrine pre-filled injector/auto-injector is available, they should follow the instructions written on the packaging

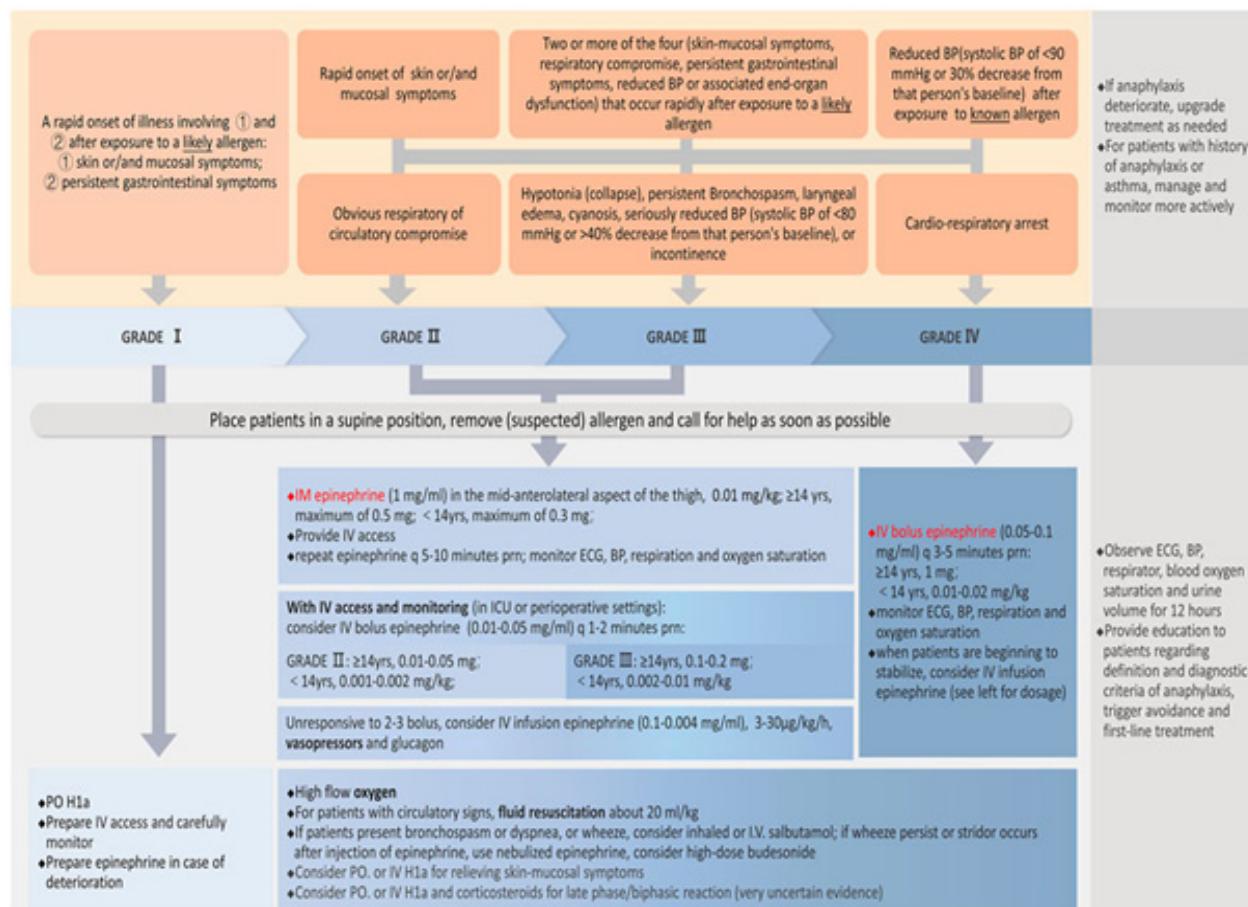
or insert. If the patient needs to be moved, should monitor vital signs (e.g., blood pressure, heart rate, temperature, respiration rate,O2 saturation). In the event of a cardiac arrest, cardiopulmonary resuscitation should be started immediately.

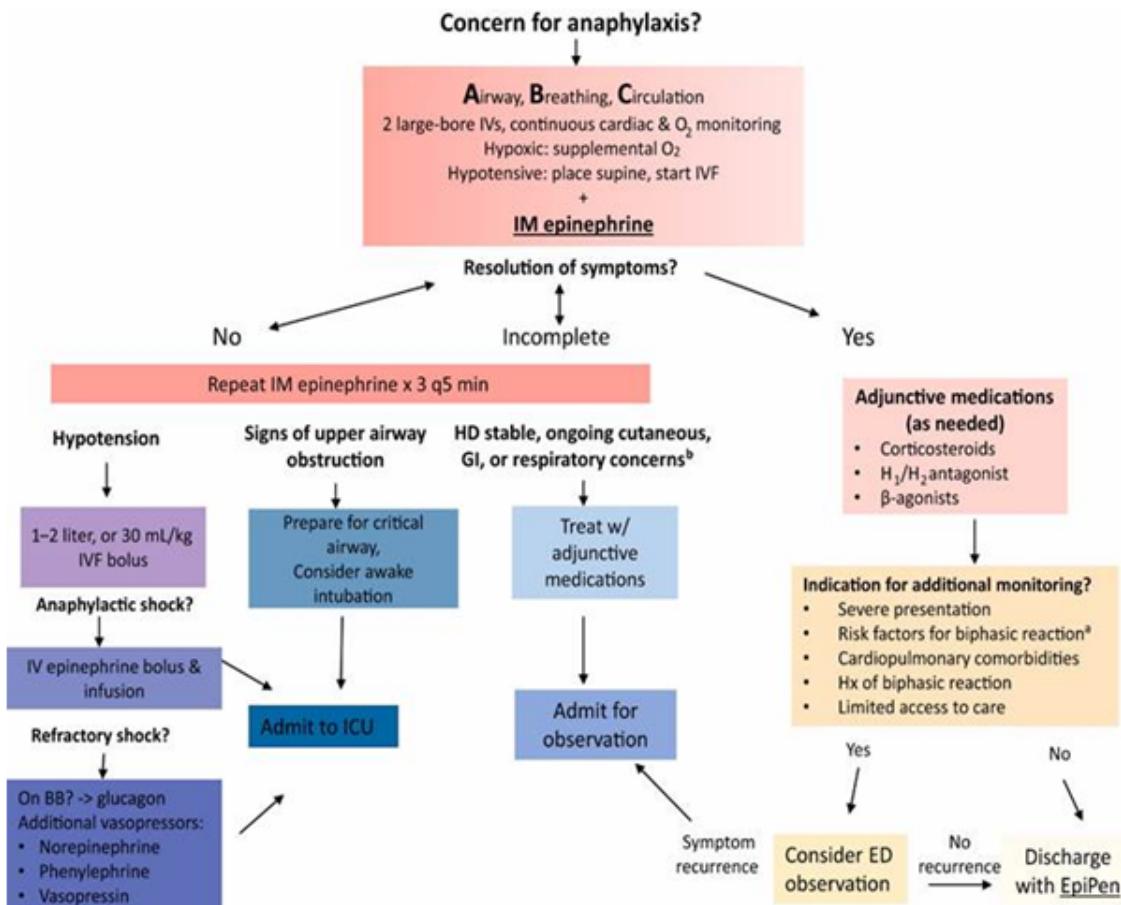
Endotracheal intubation or supraglottic airway device insertion should be performed in the case of respiratory failure or severely labored breathing due to airway edema or bronchospasm by an experienced specialist. Tracheotomy or (needle) cricothyroidotomy may be considered in the case of an emergent "cannot intubate, cannot oxygenate" scenario or other emergencies.

Patients might develop respiratory distress due to upper airway obstruction,stridor,drooling. The presence of hypotension should be considered as a warning sign of circulatory collapse and the patient should be kept in a supine position to maintain adequate circulatory and cerebral circulation. .

First-line therapy

Epinephrine:





Epinephrine is the mainstay for the management of anaphylaxis. It acts on the alpha 1 receptor , beta-1 receptor, and beta-2 receptor . The action on the alpha 1 receptor results in a decrease in mucosal edema and increases systemic vascular resistance. Action on the Beta 1 receptor results in an increase in ionotropic and chronotropic nature, and the beta 2 receptor causes vasodilation. Ideally, the route of administration of epinephrine should be IM in the anterolateral aspect of the thigh with 0.01mg/kg with a maximum dosage of 0.5mg .Dosing may be repeated every in 5–15 min if there is no response.

IV bolus epinephrine should be administered in Grade IV patients who face (imminent) cardio-respiratory arrest. Grade II and Grade III patients may be considered for IV bolus epinephrine if they already have venous access and are being monitored (i.e., ICU or perioperative patients) or unresponsive after 2-3 injections of IM epinephrine.

The dosing instructions for IV bolus of epinephrine

is as follows:

Grade IV: 1 mg for patients \geq 14 years old; 0.01–0.02 mg/kg for patients <14 years old; GRADE III: 0.1–0.2 mg for patients \geq 14 years old; 0.002–0.01 mg/kg (2–10 μ g/kg) for patients <14 years old; GRADE II: 0.01–0.05 mg for patients \geq 14 years old; 0.001–0.002 mg/kg (1–2 μ g/kg) for patients <14 years old

In Grade II or III anaphylaxis, epinephrine may be administered by IV infusion (ideally through infusion pump) when patients are unresponsive to 2-3 doses of IM/IV bolus epinephrine. These patients should already be monitored and have venous access established.

The dose of epinephrine IV infusion should be 3–30 µg/kg/h. Epinephrine should be prepared by diluting the commercial solution of 1 mg/ml (1:1000) solution to 0.004–0.1 mg/ml (1:250,000–1:10,000), in a ratio of 1:250 to 1:10.

Nebulized epinephrine administered through a

tracheal tube, or a mask with compressor, might decrease edema and obstruction in the oropharynx and larynx

SC injection of epinephrine for the emergency management of anaphylaxis is not recommended.

There is no absolute contraindication to the use of epinephrine in emergency treatment of life-threatening anaphylaxis. However caution should be used in patients with coronary heart disease, cardiomyopathy, uncontrolled hypertension, diabetes mellitus, hyperthyroidism or glaucoma. The effect of epinephrine may be potentiated in patients concurrently taking long-term monoamine oxidase inhibitors.

Inravenous Fluids:

Massive fluid shifts can happen due to increased vascular permeability, with up to 35% transfer of intravascular volume into extravascular space within minutes. Fluid resuscitation should be initiated in patients who present with orthostasis.

1. Adults should receive 1-2 litres of normal saline at the most rapid flow rate possible in the first minutes of treatment. Large volumes up to 7 litres might be required.

2. Children should receive boluses of 20 ml/kg each over 5-10 min and repeated

3. Normal saline is preferred over other solutions in most solutions. RL can potentially contribute to metabolic alkalosis, while high normal saline might cause hypercholeremic state. Dextrose is rapidly extravasated from the circulation and colloidal solutions confer no survival advantage.

Second Line Therapy

Corticosteroids:

The use of corticosteroids in the management of anaphylaxis is theoretical but it has been used for the management of anaphylaxis. Usually corticosteroids work by modulating transcription factors involved in the secretion of inflammatory cytokines that are secreted after 4-6 hrs of onset, leading to a late response. Usage of steroids is not encouraged but if it has to be used, it should be used as a second line of management and to be given after epinephrine is administered.

Antihistamines:

The role of antihistamines in the management of anaphylaxis is not clearly defined. Similar to corticosteroids, it has been seen that the concomitant use of H1 and H2 receptor blockers has been seen to reduce the urticaria and rashes most commonly seen in patients with anaphylaxis. The recommended dose of H1a are as follow: diphenhydramine, 20–50 mg for adults, 1 mg/kg for children (up to a maximum of 50 mg); chlorpheniramine, 10 mg for adults, 2.5–5 mg for children; clemastine, 2 mg for adults and 0.0125–0.025 mg/kg for children.

Inhaled Bronchodilators:

It has been usually seen that patients having an anaphylaxis attack often experience bronchospasm and it has been seen that use of inhaled beta agonists or bronchodilators like albuterol or inhalational anticholinergics is the choice of the drug. Salbutamol can be inhaled. The dose for salbutamol is 2–12 puffs by metered dose inhaler with a spacer; or 2–5 mg in 3 ml of saline by nebulizer; or 0.1–0.4 mg administered intravenously.

REFRACTORY ANAPHYLAXIS

Patients with anaphylaxis who do not respond to epinephrine typically have a history of beta-

Agent	Route of administration
Hydrocortisone	IV or IM
Methylprednisolone	IV or IM
Dexamethasone	IV or IM

blocker use, which promotes an increase in the production of inflammatory mediators. Glucagon administration has been shown to outperform adenyl cyclase and improve ionotropic and chronotropic effects. Glucagon usually causes vomiting and care should be taken regarding securing the patient's airway. For refractory anaphylaxis, noninvasive ventilation should be performed routinely and invasive ventilation should be performed when indicated. Cardiopulmonary resuscitation should be prepared. Vasopressors combined with epinephrine may improve the outcome in in-hospital cardiac arrest patients, some guidelines suggest the use of vasopressor might be beneficial.

Vasopressors:

In patients with refractory anaphylactic shock infusion of Norepinephrine has to be considered, which acts both on the alpha 1 receptor and provides better protection from tachyphylaxis that is most commonly seen with epinephrine. Alternatively, Vasopressin can also be used in patients, which binds to the v1 receptor in smooth muscle that leads to vasoconstriction. It inactivates ATP sensitive potassium channels that lead to vasoconstriction and should be considered in the case of refractory hypotension.

Complications

- Wheeze
- Stridor
- Hypoxemia
- Hypotension
- End-organ dysfunction and
- Death

Follow Up

All cases of drug-induced anaphylaxis should be reported to an ADR surveillance system. The key preventive measure is to avoid allergens. Prophylactic medications cannot be routinely used in the general population.

Patients should referred to allergist and immunologist to assist in the determination of inciting agents and prevention of future reoccurrences. Once the patient is stabilized, short-term desensitization procedures can be undertaken. Immunotherapy may prevent anaphylaxis in long-term anaphylaxis management, which should be performed with the supervision of experienced allergists

At discharge, patients should always be provided with an epinephrine auto-injector and instructed on how to use it. Health care providers should teach patients and/or caregivers about anaphylaxis including diagnostic criteria, avoidance of potential triggers, and first-line treatments.

Despite awareness of the seriousness of anaphylaxis, and treatment of anaphylaxis is not optimal. At least 1500 die each year from a condition that can be treated and even prevented. it is important that all healthcare workers are prepared to deal with and possess the knowledge and skills to administer epinephrine and coordinate with other team members to arrange the appropriate follow-up care, leading to better patient outcomes.

References

- 1) Clinical Practice Guideline for the Emergency Management of Anaphylaxis (2020) doi: 10.3389/fphar.2022.845689
- 2) Overview of Allergy and Anaphylaxis, Med Clin North Am. 2022 February ; 40(1): 1–17. doi:10.1016/j.emc.2021.08.007
- 3) Adult anaphylaxis: A state-of-the-art review, European Journal of Internal Medicine 100 (2022) 5- 12
- 4) Anaphylaxis Kevin McLendon; Britni T. Sternard. Treasure Island (FL): StatPearls Publishing; 2022 Jan



Pulmonary Thromboembolism

Dr. Srirang Abkari

Consultant Physician

Udai Omni Hospital, Hyderabad

Acute pulmonary embolism (PE) is a form of venous thromboembolism (VTE) that is quite common in clinical practice. It can sometimes even be fatal. The clinical presentation of a patient who develops PE is variable and often nonspecific making the diagnosis challenging and requiring a high degree of suspicion. PE is known as "the Great Masquerader," making diagnosis difficult. The evaluation of patients with suspected PE should be efficient and systematic. It ensures a proper diagnosis so that therapy can be administered quickly to reduce the associated morbidity and mortality.

Pulmonary embolus (PE) refers to obstruction of the pulmonary artery or one of its branches by material (eg, thrombus, tumor, air, or fat) that originated elsewhere in the body.

It can be classified in the following ways:

A. Based on the temporal pattern of presentation

- **Acute:** develop symptoms and signs immediately after obstruction of pulmonary vessels.
- **Subacute:** present subacutely within days or weeks following the initial event.
- **Chronic:** slowly develop symptoms of pulmonary hypertension over many years (ie, chronic thromboembolic pulmonary hypertension; CTEPH).

B. Based on the presence or absence of hemodynamic stability

- (i) Hemodynamically unstable PE ("massive" or "high-risk" PE)

It results in hypotension which is defined as a systolic blood pressure (SBP) <90 mmHg or a drop in SBP of ≥40 mmHg from baseline for a period >15 minutes or hypotension that requires vasopressors or inotropic support and is not explained by other causes such as sepsis, arrhythmia, left ventricular dysfunction from acute myocardial ischemia or infarction, or hypovolemia. Although hemodynamically unstable PE is often caused by large (ie, massive) PE, it can sometimes be due to small PE in patients with underlying cardiopulmonary disease.

(ii) Hemodynamically stable PE

- Submassive or intermediate-risk PE: associated right ventricular strain
- Low-risk PE: no evidence of right ventricular strain.

It is important to differentiate between hemodynamically stable and unstable PE because patients with hemodynamically unstable PE are more likely to die from obstructive shock (ie, severe right ventricular failure). Also it is pertinent to note that death from hemodynamically unstable PE often occurs within the first two hours, and the risk remains elevated for up to 72 hours after presentation.

C. Based on the anatomic location

- **saddle**
- **lobar**
- **segmental**
- **subsegmental**
- **unilateral or bilateral**

D. Based on the presence or absence of symptoms

- Symptomatic
- Asymptomatic

Epidemiology:

The incidence of pulmonary embolism (PE) ranges from 39 to 115 per 100000 population annually; for DVT, the incidence ranges from 53 to 162 per 100,000 people.

PATHOGENESIS AND PATHOPHYSIOLOGY

The pathogenesis of pulmonary embolism (PE) is similar to that which underlies the generation of thrombus (ie, Virchow's triad). Virchow's triad consists of venous stasis, endothelial injury, and a hypercoagulable state.

Risk factors

Can be classified as

- Inherited
- Acquired

- (i) **Provoking** (eg, recent surgery, trauma, immobilization, initiation of hormone therapy, active cancer)
- (ii) **Non-provoking** (eg, obesity, heavy cigarette smoking)

Risk factors for the development of venous thrombosis

- Inherited thrombophilia
- Factor V Leiden mutation
- Prothrombin G20210A mutation
- Protein S deficiency
- Protein C deficiency
- Antithrombin deficiency

Other disorders and risk factors

- Presence of a central venous catheter
- Malignancy
- Surgery, especially orthopedic

- Trauma
- Immobilization
- Pregnancy
- Oral contraceptives
- Hormone replacement therapy
- Certain cancer therapies (eg, tamoxifen, thalidomide, lenalidomide, asparaginase)
- Heart failure
- Congenital heart disease
- Antiphospholipid syndrome
- Older age (e>65 years)
- Obesity
- Severe liver disease
- Myeloproliferative neoplasms
- Polycythemia vera
- Essential thrombocythemia
- Paroxysmal nocturnal hemoglobinuria
- Inflammatory bowel disease
- Nephrotic syndrome

Source: Most emboli are thought to arise from lower extremity proximal veins (iliac, femoral, and popliteal) and more than 50 percent of patients with proximal vein deep venous thrombosis (DVT) have concurrent PE at presentation.

Pathophysiologic response to PE

- (i) Infarction
- (ii) Abnormal gas exchange: Most common is hypoxemia (decreased arterial P_o_2) and an increased alveolar-arterial O_2 tension gradient, which represents the inefficiency of O_2 transfer across the lungs. Anatomic dead space increases because breathed gas does not enter gas exchange units of the lung. Physiologic dead space increases because ventilation to gas exchange units exceeds venous blood flow through the pulmonary capillaries. Thus there is impaired gas exchange due to increased alveolar dead space from vascular obstruction, hypoxemia from alveolar hypoventilation relative to perfusion in the non-obstructed lung, right-to-left shunting,

and impaired carbon monoxide transfer due to loss of gas exchange surface.

- (iii) Cardiovascular compromise
- (iv) Increased pulmonary vascular resistance due to vascular obstruction or platelet secretion of vasoconstricting neurohumoral agents such as serotonin. Release of vasoactive mediators can produce ventilation-perfusion mismatching at sites remote from the embolus, thereby accounting for a potential discordance between a small PE and a large alveolar-arterial O₂ gradient.
- (v) Alveolar hyperventilation due to reflex stimulation of irritant receptors.
- (vi) Increased airway resistance due to constriction of airways distal to the bronchi.
- (vii) Decreased pulmonary compliance due to lung edema, lung hemorrhage, or loss of surfactant.

Clinical presentation

Symptoms and signs of acute pulmonary embolism

Symptom

- Asymptomatic
- Dyspnea
- Pleuritic chest pain
- Cough
- Hemoptysis
- Syncope
- Calf or thigh pain and/or swelling
- Wheezing

Signs

- Tachypnea
- Rales
- Tachycardia
- Fourth heart sound
- Accentuated pulmonic component of second heart sound

- Circulatory collapse
- Jugular venous distension
- Parasternal heave
- Fever, mimicking pneumonia
- Decreased breath sounds
- Calf or thigh swelling, erythema, edema, tenderness, palpable cords

Diagnostic approach to patients with suspected PE

Wells criteria and modified Wells criteria: Clinical assessment for pulmonary embolism

Probability	Score
Traditional clinical probability assessment (Wells criteria)	
High	>6.0
Moderate	2.0 to 6.0
Low	<2.0
Simplified clinical probability assessment (Modified Wells criteria)	
PE likely	>4.0
PE unlikely	<4.0

Since symptoms of PE are very nonspecific, The Pulmonary Embolism Rule-out Criteria (PERC) was developed for emergency department patients to select patients whose likelihood of having PE is so low that diagnostic workup should

not even be initiated. They constitute variables significantly associated with the *absence* of PE.

The PERC rule has eight criteria:

- Age <50 years
- Heart rate <100 beats per minute
- Oxyhemoglobin saturation ≥95 percent
- No hemoptysis
- No estrogen use
- No prior DVT or PE
- No unilateral leg swelling
- No surgery/trauma requiring hospitalization within the preceding four weeks

Patients having a low probability of PE who fulfill all eight criteria, the likelihood of PE is sufficiently low that further testing is not indicated.

PERC is only valid in clinical settings with a low prevalence of PE (<15 percent). In hospital settings with a higher prevalence of PE (>15 percent), the PERC-based approach has substantially weaker predictive value. Therefore, it should not be used in patients with an intermediate or high suspicion for PE or for inpatients suspected as having PE. (Figures)

Diagnostic Workup

Arterial Blood Gas (ABG) Analysis

Unexplained hypoxemia with a normal chest radiograph should raise the clinical suspicion for pulmonary embolism (PE). Widened alveolar-arterial gradient for oxygen, respiratory alkalosis, and hypocapnia are commonly seen findings on ABG, as a pathophysiological response to pulmonary embolism. It is important to note that hypercapnia, respiratory, or lactic acidosis is not common but can be present in patients with massive PE associated with obstructive shock and respiratory arrest.

Brain Natriuretic Peptide (BNP)

Elevated BNP has limited diagnostic importance in patients suspected of having PE. Right ventricle

pressure overload because of acute PE is associated with more myocardial stretch, which then releases B-type natriuretic peptide (BNP) and N-terminal (NT)-proBNP. Thus, the levels of natriuretic peptides in blood reflect the severity of RV dysfunction in acute PE.

Troponin

Serum troponin I and T levels are beneficial prognostically but not diagnostically. As markers of right ventricular dysfunction, troponin levels are elevated in 30 to 50 percent of patients with moderate to large PE and are linked to clinical deterioration and death after PE.

D-dimer

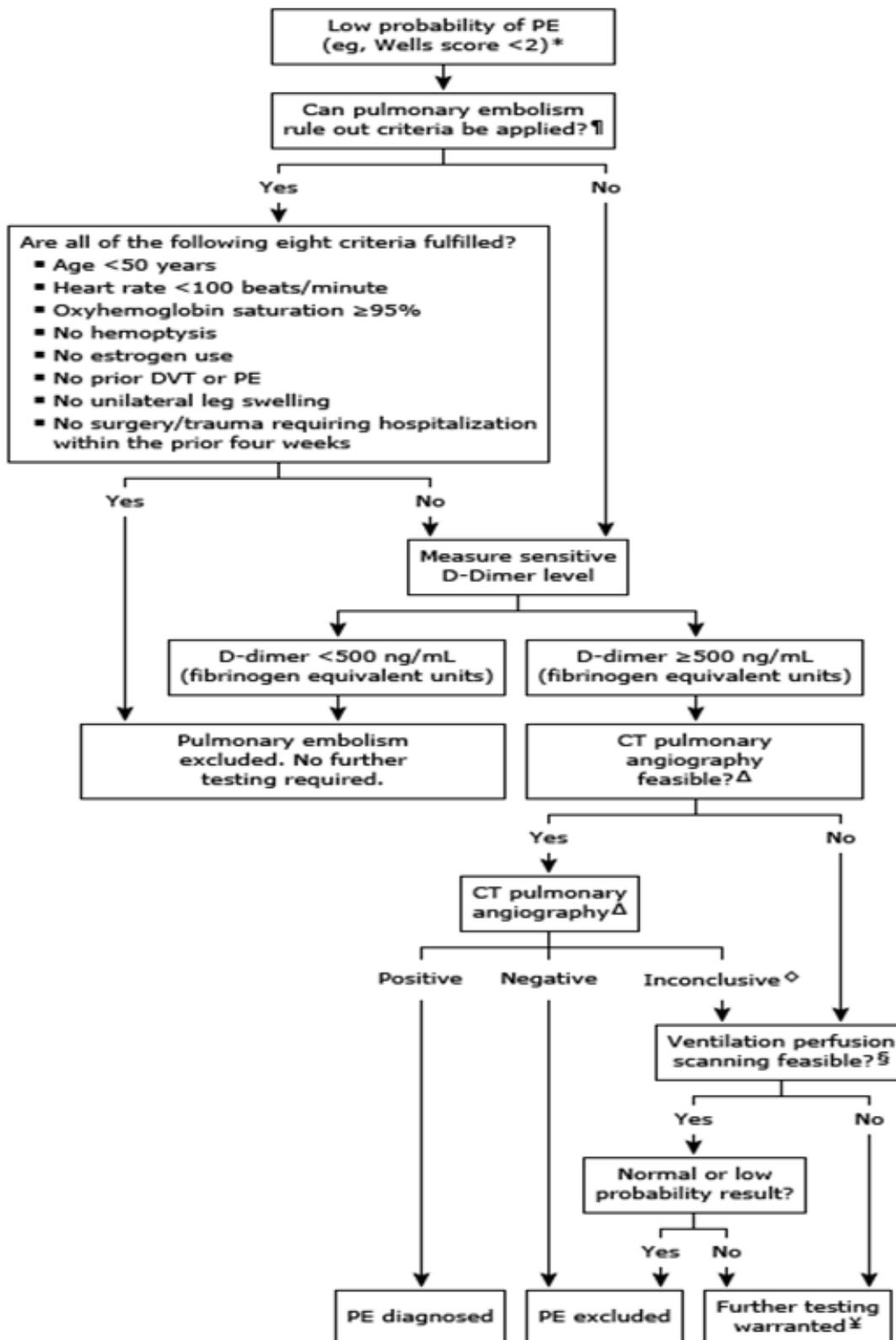
D-dimer levels are elevated in plasma whenever there is an acute thrombotic process in the body because of the activation of coagulation and fibrinolysis pathways at the same time. D-dimer testing has high negative predictive value; hence, a normal D-dimer level makes acute PE or DVT unlikely. But since the positive predictive value of elevated D-dimer levels is low, D-dimer testing is not useful for confirmation of PE. The quantitative enzyme-linked immunosorbent assay (ELISA) has a diagnostic sensitivity of at least 95%. It can be used to exclude the diagnosis of PE in patients with either low or intermediate pretest probability. A negative ELISA D-dimer, along with low clinical probability, can exclude PE without further testing in approximately 30% of suspected patients.

The specificity of D-dimer decreases steadily with age to approximately 10% in patients greater than 80 years of age. The formula is age (years) × 10 mcg/L for patients more than 50 years of age. Example: Patient age 75 = age-adjusted d-dimer of 750 mcg/L.

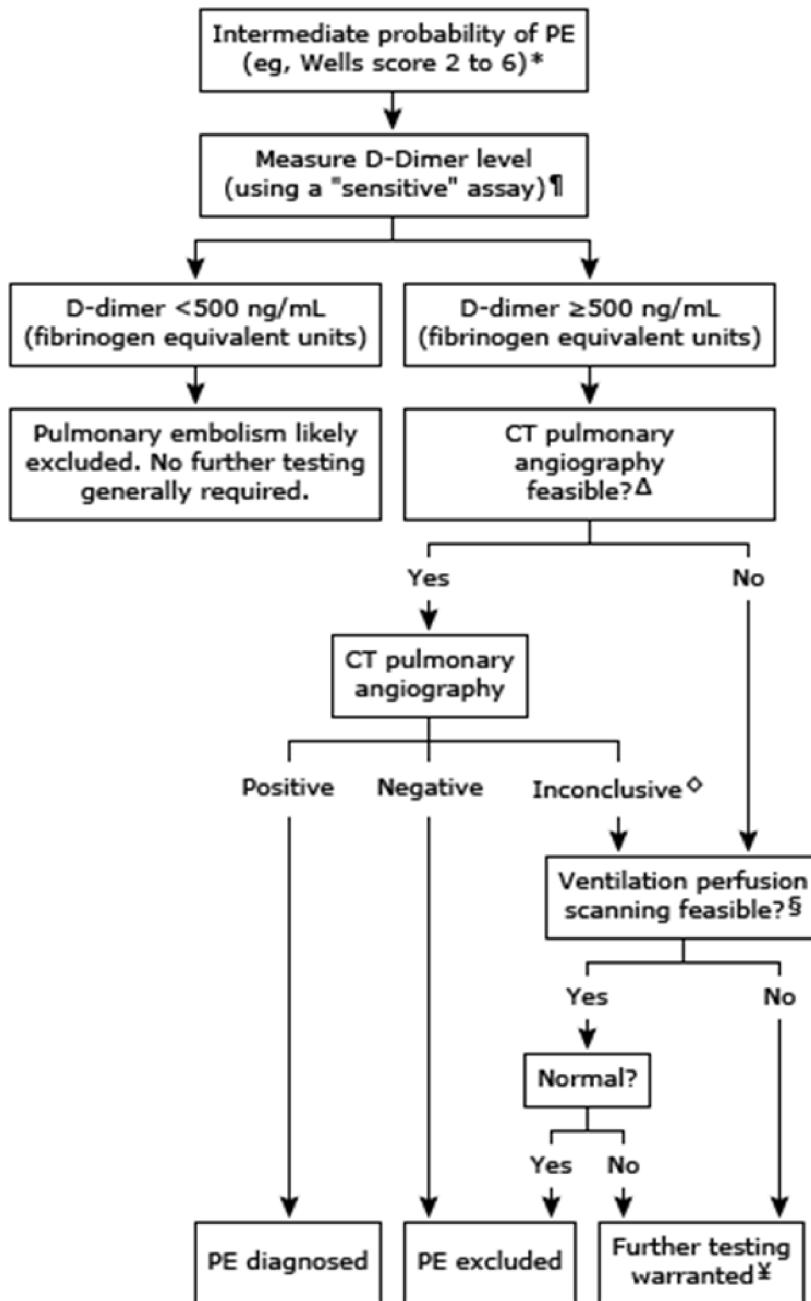
Electrocardiography (ECG)

ECG abnormalities, in patients with suspected PE, are nonspecific. The most common ECG findings in PE are sinus tachycardia and nonspecific ST-segment and T-wave changes, S1Q3T3 pattern, Anterior precordial T Wave inversion, right

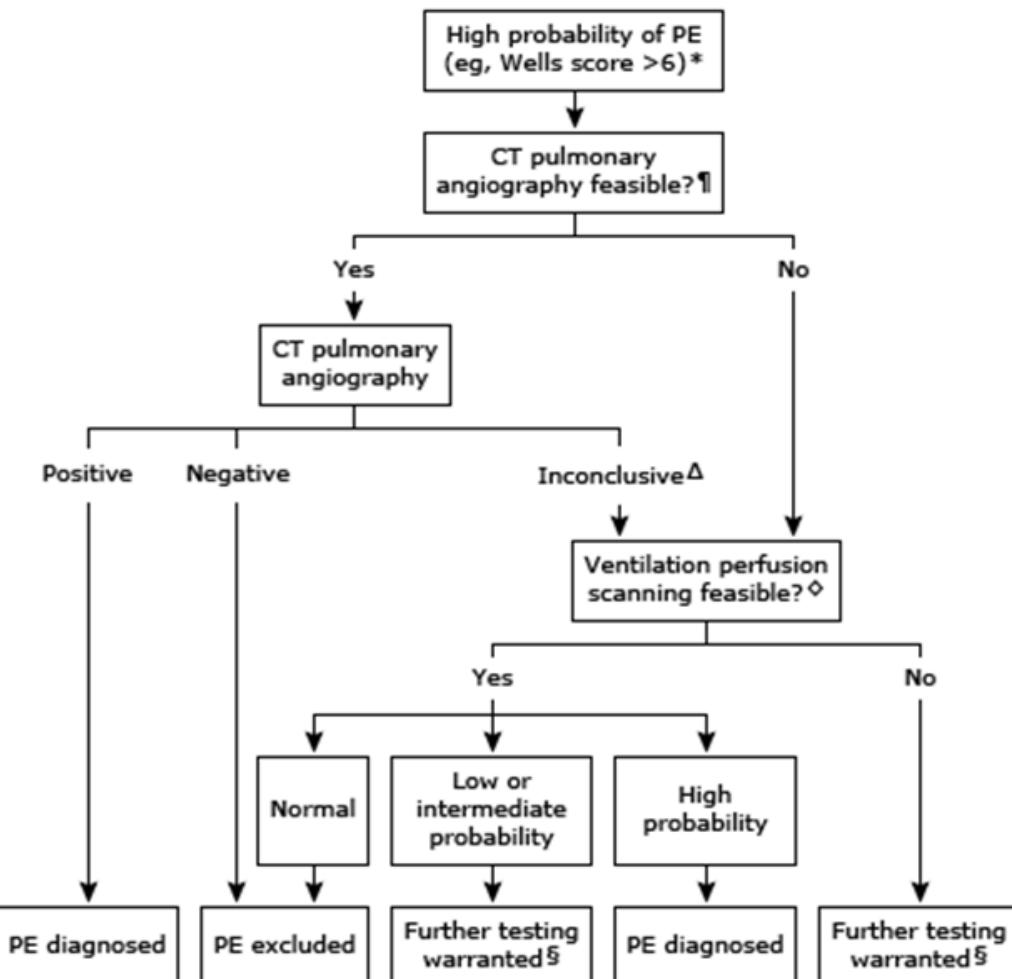
Evaluation of the nonpregnant adult with low probability of pulmonary embolism



Evaluation of the nonpregnant adult with intermediate probability of pulmonary embolism



Evaluation of the nonpregnant adult with high probability of pulmonary embolism



ventricular strain, and new incomplete right bundle branch block are uncommon.

Chest Radiograph (CXR)

In PE, CXR is usually normal or might show nonspecific abnormalities such as atelectasis or effusion. It helps to rule out alternative diagnoses in patients presenting with acute dyspnea.

Hampton's hump is a shallow, hump-shaped opacity on CXR in the periphery of the lung, with its base lying against the pleural surface and hump towards the hilum. Fig1. Westermark's sign is the sharp cut-off of pulmonary vessels with distal hypoperfusion in a segmental distribution within the lung; both of these findings are rare but specific for acute PE. 'Westermark sign' may be seen in up to 2% of the cases. This finding is a

result of a combination of dilation of the pulmonary artery proximal to the thrombus and the collapse of the distal vasculature.

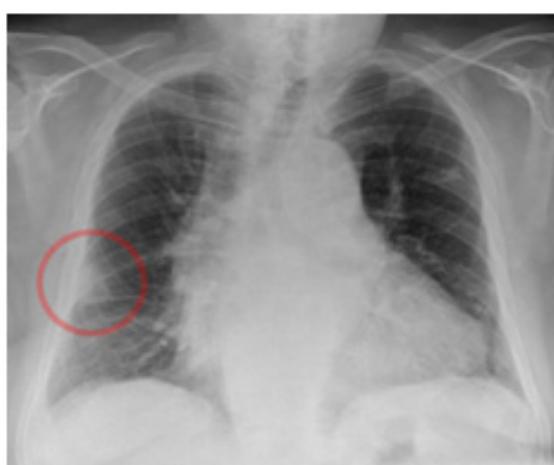


Fig1: Hampton's hump

Computed Tomographic Pulmonary Angiography (CTPA) fig2

Multidetector CTPA is the diagnostic modality of choice for patients with suspected PE. It allows appropriate visualization of the pulmonary arteries down to the subsegmental level. The PIOPED (Prospective Investigation On Pulmonary Embolism Diagnosis) II study showed a sensitivity of 83% and a specificity of 96% for CTPA in PE diagnosis. PIOPED II also highlighted the pretest clinical probability influence on the predictive value of CTPA. Therefore, providers should consider further testing in case of discordance between clinical judgment and the CTPA result.

CTPA may be relatively contraindicated in moderate to severe iodinated contrast allergy or renal insufficiency (eGFR less than 30 mL/min per 1.73-meter square). The risk of these contraindications must be measured against the clinical significance of performing the CTPA examination and the availability of other imaging modalities (e.g., V/Q scan). If clinically feasible, CTPA should be postponed for premedication for a history of allergy or intravenous hydration for renal insufficiency.

CTPA can detect RV enlargement and other indicators of RV dysfunction. Enlarged RV has prognostic value, and it is supported by the results of a prospective multicentre cohort study in 457 patients. In that study, RV enlargement (RV/LV ratio ≥ 0.9) was a strong and independent predictor of a severe in-hospital outcome, both in the overall population and in hemodynamically stable patients.

Lung Scintigraphy

The planar ventilation/perfusion scan (V/Q scan) is an established diagnostic test for suspected PE. V/Q scanning is mostly performed for patients in whom CTPA is contraindicated or inconclusive, or when additional testing is needed. A normal chest radiograph is usually required before V/Q scanning. Scans performed on patients with abnormal chest radiographs are most likely to be false positives because the images do not

appear normal or low probability of PE in such patients.

For those with a normal chest radiograph, V/Q scanning remains the test of choice for the diagnosis of PE in pregnancy. Other groups of patients include those who have a history of contrast medium-induced anaphylaxis and patients with severe renal failure.

Planar lung scan results are frequently classified into three-tiers: normal scan (excluding PE), high-probability scan (considered diagnostic of PE in most patients), and nondiagnostic scan. An analysis from the PIOPED II study advocated that a high-probability V/Q scan can confirm PE. However, the positive predictive value of a high-probability V/Q scan is not enough to confirm the PE diagnosis in patients with a low clinical probability. The high frequency of nondiagnostic scans is a limitation because they indicate the necessity for further diagnostic testing.

Pulmonary Angiography

In pulmonary angiography, contrast is injected via a catheter introduced into the right heart under fluoroscopy, which was the gold standard in the past for the diagnosis of PE. The diagnosis of acute PE is made on the evidence of a thrombus either as amputation of a pulmonary arterial branch or filling defect. With the widespread emergence of CTPA, pulmonary angiography is infrequently used and reserved for rare circumstances for patients with a high clinical probability of PE, in whom CTPA or V/Q scanning is nondiagnostic. Pulmonary angiography seems to be inferior to CTPA, and its results are operator dependent and highly variable. Therefore, catheter-based pulmonary angiography is performed in patients who need therapeutic benefit since it helps with diagnosis as well as therapeutic interventions aimed at clot lysis.

Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) has been assessed for several years regarding suspected PE. However, the results of large-scale

studies show that this technique, although promising, is not recommended as a first-line test for the diagnosis of PE due to its low sensitivity, low availability in most emergency settings, and the high proportion of inconclusive MRA scans. But it may be an imaging option for diagnosis of PE in patients in whom neither CTPA nor V/Q scan can be performed. Potential advantages include no exposure to radiation.

Echocardiography

Transthoracic echocardiography can very rarely diagnose PE definitively when the thrombus is visualized in the proximal pulmonary arteries. The diagnosis of PE on echocardiography is supported by the presence of clot in the right heart or new right heart strain, especially in hemodynamically unstable patients with suspected PE wherein echocardiogram may be useful to establish a possible diagnosis and justify the emergency use of thrombolytic therapy.

There are significant considerations with using echocardiography to establish a diagnosis of PE. Given the peculiar shape of the RV, there is no single echocardiographic parameter that gives quick and accurate information on RV size or function. That is why echocardiographic criteria for the diagnosis of PE have varied between different studies. Because of the negative predictive value of 40% to 50%, a negative result cannot exclude PE. On the other hand, signs of RV overload or dysfunction may also be present without acute PE, and may be due to coexisting cardiac or respiratory disease.

RV dilation is seen in 25% or more of patients with PE on echo and is useful for risk stratification of the disease.[More specific echocardiography findings confer a high positive predictive value for PE, even in the presence of preexisting cardiorespiratory illness. This includes, the combination of a pulmonary ejection acceleration time (measured in the RV outflow tract) less than 60 ms with a peak systolic tricuspid valve gradient less than 60 mmHg ('60/60' sign), or McConnell sign (with depressed contractility of the RV free

wall compared to the RV apex), is suggestive of PE.. An RV/LV diameter ratio 1.0 or more and tricuspid annular plane systolic excursion (TAPSE) less than 16 mm are the findings for which an association with unfavorable prognosis has most frequently been reported.

Compression Ultrasonography (US)

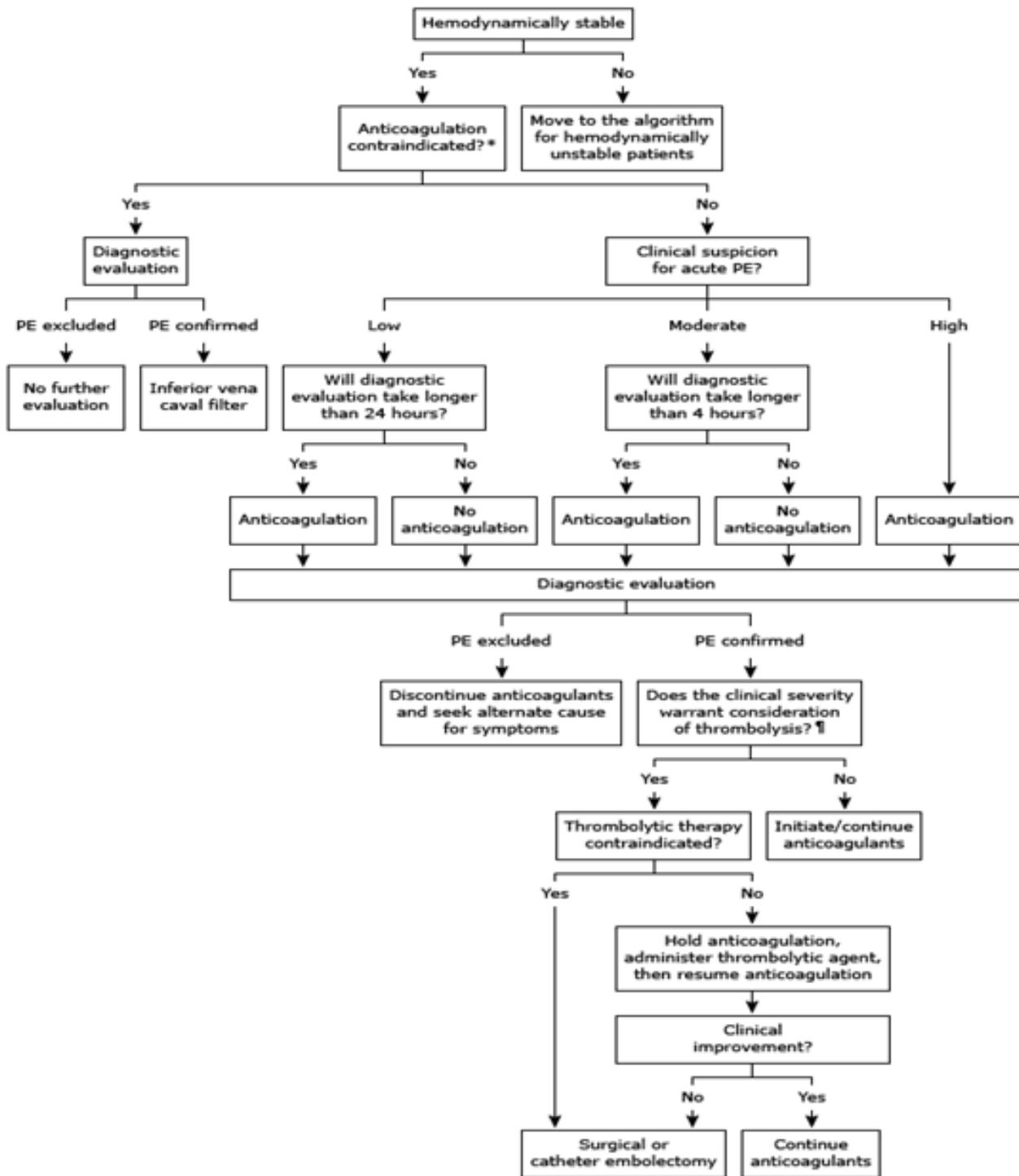
PE originates from a lower limb DVT in a majority of patients, and only rarely from upper-limb DVT (mostly following venous catheterization). In one study, DVT was found in 70% of patients with proven PE. Compression US has a sensitivity of more than 90% and a specificity of about 95% for proximal symptomatic DVT. A finding of proximal DVT in patients suspected of having PE is considered sufficient to warrant anticoagulant treatment without further testing. It is important to note that, due to the low sensitivity of compression ultrasonography, it is reserved for patients in whom definitive imaging (e.g., CTPA, V/Q scanning) is contraindicated or indeterminate

TREATMENT

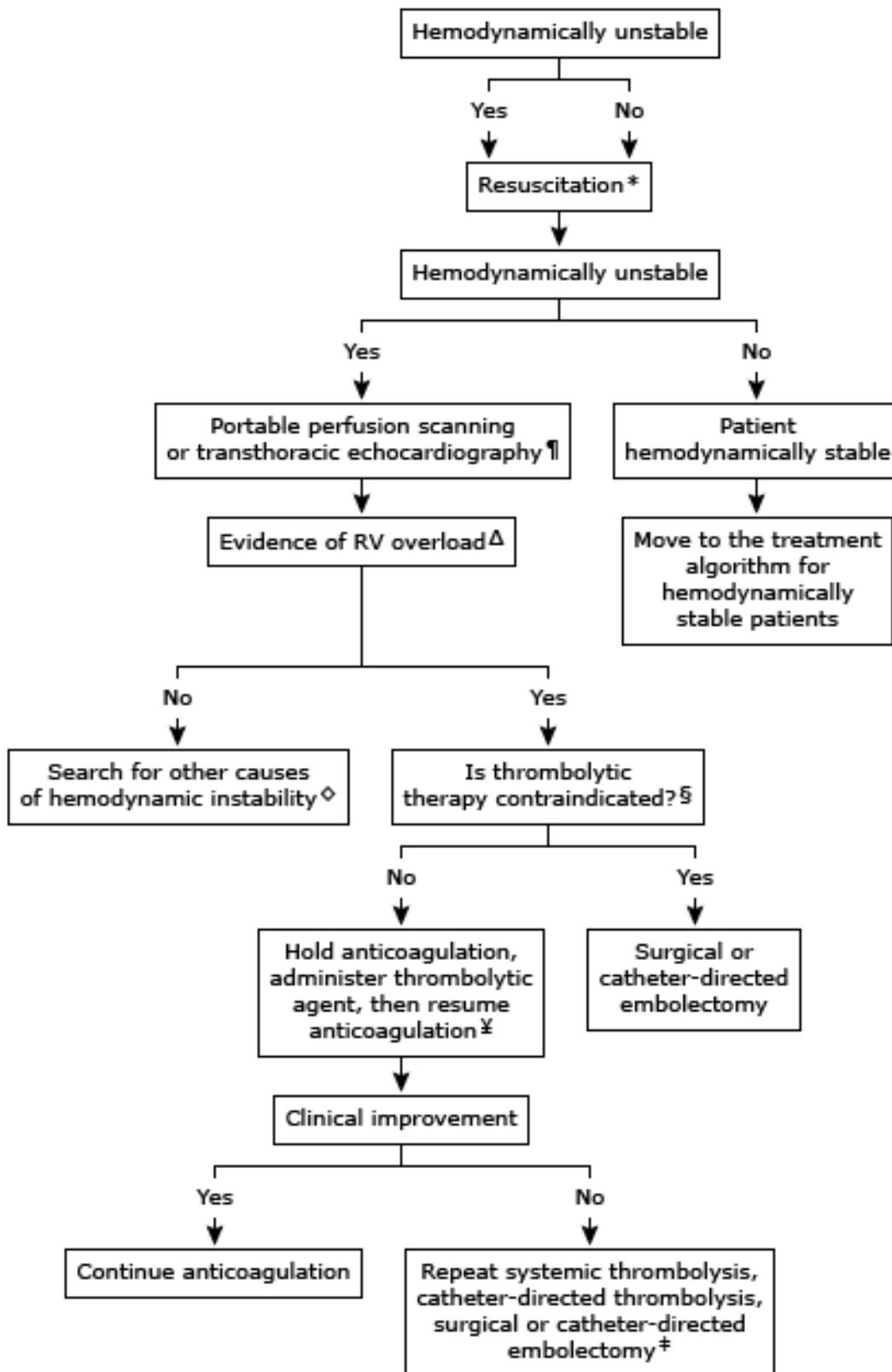
Initial resuscitative therapy should focus upon oxygenating and stabilizing the patient. Resuscitative therapy may range from supplemental oxygen to ventilatory and hemodynamic support. Intravenous fluid resuscitation should be limited, as further distention of an already dilated right ventricle (RV) can worsen hemodynamics. If possible, endotracheal intubation should be avoided, as positive pressure ventilation can reduce preload and compress the failing RV, leading to hemodynamic collapse.

Once the diagnosis is made, the mainstay of therapy for patients with confirmed PE is anticoagulation, depending upon the risk of bleeding. When the pre-test probability of PE is high or diagnostic imaging will be delayed, anticoagulation is sometimes started before a diagnosis of PE is confirmed.

Treatment algorithm for hemodynamically stable patients with suspected pulmonary embolism (PE)



Treatment algorithm for hemodynamically unstable patients with suspected pulmonary embolism (PE)



Anticoagulation for VTE

Immediate Parenteral Anticoagulation

Unfractionated heparin, bolus and continuous infusion, to achieve aPTT two to three times the upper limit of the laboratory normal, or
Enoxaparin 1 mg/kg twice daily with normal renal function, or
Dalteparin 200 U/kg once daily or 100 U/kg twice daily, with normal renal function, or
Tinzaparin 175 U/kg once daily with normal renal function, or
Fondaparinux weight-based once daily; adjust for impaired renal function

Warfarin Anticoagulation

Usual start dose is 5 mg
Titrate to INR, target 2.0–3.0
Continue parenteral anticoagulation for a minimum of 5 days and until two sequential INR values, at least 1 day apart, achieve the target INR range.

ANTICOAGULATION

Anticoagulation is the foundation for successful treatment of DVT and PE. Immediately effective anticoagulation is initiated with a parenteral drug: unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), or fondaparinux. One should use a direct thrombin inhibitor—argatroban, lepirudin, or bivalirudin—in patients with proven or suspected heparin-induced thrombocytopenia. Parenteral agents are continued as a transition or “bridge” to stable, long-term anticoagulation with a vitamin K antagonist. Warfarin requires 5–7 days to achieve a therapeutic effect. During that period, one should overlap the parenteral and oral agents. After 5–7 days of anticoagulation, residual thrombus begins to endothelialize in the vein or pulmonary artery. Newer oral anticoagulants (NOACs) can also be used for anticoagulation in PE. In patients with PE and a systolic blood pressure of 90 mm Hg or higher, compared with heparin combined with a vitamin K antagonist such as warfarin followed by warfarin alone, direct oral anticoagulants such as apixaban, edoxaban, rivaroxaban, or dabigatran, are noninferior for treating PE and have a 0.6% lower rate of bleeding. However, anticoagulants do *not* directly dissolve thrombus that already exists.

Duration of Anticoagulation Patients with PE after surgery, trauma, or estrogen exposure (from oral contraceptives, pregnancy, or postmenopausal therapy) ordinarily have a low rate of recurrence after 3–6 months of anticoagulation. For DVT isolated to an upper extremity or calf that has been provoked by surgery, trauma, estrogen, or an indwelling central venous catheter or pacemaker, 3 months of anticoagulation suffices. For provoked proximal leg DVT or PE, 3 to 6 months of anticoagulation is sufficient. For patients with cancer and VTE, the consensus is to prescribe 3–6 months of LMWH as monotherapy without warfarin and to continue anticoagulation indefinitely unless the patient is rendered cancer-free. However, there is uncertainty whether subsequent anticoagulation should continue with LMWH or whether the patient should be placed on warfarin. Among patients with idiopathic, unprovoked VTE, the recurrence rate is high after cessation of anticoagulation. VTE that occurs during long-haul air travel is considered unprovoked. It appears that unprovoked VTE is often a chronic illness, with latent periods between flares of recurrent episodes. American College of Chest Physicians (ACCP) guidelines recommend considering anticoagulation for an

indefinite duration with a target INR between 2 and 3 for patients with idiopathic VTE. An alternative approach after the first 6 months of anticoagulation is to reduce the intensity of anticoagulation and to lower the target INR range to between 1.5 and 2. Counterintuitively, the presence of genetic mutations such as heterozygous factor V Leiden and prothrombin gene mutation do not appear to increase the risk of recurrent VTE. However, patients with moderate or high levels of anticardiolipin antibodies probably warrant indefinite-duration anticoagulation even if the initial VTE was provoked by trauma or surgery.

INFERIOR VENA CAVAL (IVC) FILTERS

These block the path of travel of emboli and prevent them from entering the pulmonary circulation. The two principal indications for insertion of an IVC filter are

- (1) Active bleeding that precludes anticoagulation and
- (2) Recurrent venous thrombosis despite intensive anticoagulation.

Prevention of recurrent PE in patients with right heart failure who are not candidates for fibrinolysis and prophylaxis of extremely high-risk patients are "softer" indications for filter placement. The filter itself may fail by permitting the passage of small- to medium-size clots. Large thrombi may embolize to the pulmonary arteries via collateral veins that develop. A more common complication is caval thrombosis with marked bilateral leg swelling. Retrievable filters are preferred, such that once the contraindication has resolved, the filter can be removed, and patients should be anticoagulated.

MAINTAINING ADEQUATE CIRCULATION For patients with massive PE and hypotension, one should administer 500 mL of normal saline. Additional fluid should be infused with extreme caution because excessive fluid administration exacerbates RV wall stress, causes more profound RV ischemia, and worsens LV compliance and filling by causing further interventricular septal

shift toward the LV. Dopamine and dobutamine are first line inotropic agents for treatment of PE-related shock. There should be a low threshold for initiating these pressors. Often, a "trial-and-error" approach works best; one should consider norepinephrine, vasopressin, or phenylephrine.

FIBRINOLYSIS

Successful fibrinolytic therapy rapidly reverses right heart failure and may result in a lower rate of death and recurrent PE by

- (1) Dissolving much of the anatomically obstructing pulmonary arterial thrombus,
- (2) Preventing the continued release of serotonin and other neurohumoral factors that exacerbate pulmonary hypertension, and
- (3) Lysing much of the source of the thrombus in the pelvic or deep leg veins, thereby decreasing the likelihood of recurrent PE.

Once it is decided that thrombolytic therapy is indicated, the method of administration (eg, catheter-directed versus systemic) and dosing (full or reduced dose, infusion versus bolus) depend on factors including hemodynamic instability, risk of bleeding, available expertise, oxygen requirement, and extent of the emboli

Indications and potential indications for thrombolytic therapy in venous thromboembolism

Indication

High-risk (massive) PE (ie, presence of hypotension related to PE)*

Potential indication

Patients with severe right ventricular dysfunction due to PE (ie, intermediate risk PE) Others:

Presence of severe hypoxemia (particularly in those with a contribution from concomitant cardiopulmonary disease)

Patients with acute PE who appear to be decompensating but are not yet hypotensive

Extensive clot burden

* This indication is widely accepted; the other potential indications require careful review of the risks of thrombolytic therapy and potential benefits.

Dosing (continuous infusion)

Full-dose IV thrombolytic infusion regimens are the most common method of administering these agents. Recombinant tPA (eg, alteplase, tenecteplase), streptokinase (SK), and recombinant human urokinase (UK), are the best studied thrombolytic agents for the treatment of acute PE. No agent has proven to be superior. In view of a shorter infusion time, tPA (in particular alteplase) is the most common agent used for patients with acute PE.

The US Food and Drug Administration-approved dosing regimen for IV tPA (alteplase) is 100 mg administered over two hours. In more urgent situations (eg, impending cardiac arrest), it is appropriate to administer tPA as a bolus, as an infusion over 15 minutes, or as a 20 mg IV bolus followed by an infusion of 80 mg over the next two hours. Patients appear to respond to fibrinolysis for up to 14 days after the PE has occurred. Careful screening of patients for contraindications to fibrinolytic therapy is the best way to minimize bleeding risk

Contraindications to fibrinolytic therapy for deep venous thrombosis or acute pulmonary embolism

Absolute contraindications

- Prior intracranial hemorrhage
- Known structural cerebral vascular lesion
- Known malignant intracranial neoplasm
- Ischemic stroke within three months (excluding stroke within three hours*)
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head trauma or facial trauma within three months

Relative contraindications

- History of chronic, severe, poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (SBP >180 mmHg or DBP >110 mmHg)
- History of ischemic stroke more than three months prior
- Traumatic or prolonged (>10 minute) CPR or major surgery less than three weeks
- Recent (within two to four weeks) internal bleeding
- Noncompressible vascular punctures
- Recent invasive procedure
- For streptokinase/anistreplase - Prior exposure (more than five days ago) or prior allergic reaction to these agents
- Pregnancy
- Active peptic ulcer
- Pericarditis or pericardial fluid
- Current use of anticoagulant (eg, warfarin sodium) that has produced an elevated international normalized ratio (INR) >1.7 or prothrombin time (PT) >15 seconds
- Age >75 years
- Diabetic retinopathy

Patients with contraindications – For those who are unstable due to PE and have contraindications to thrombolysis or are at high risk of bleeding or for patients who fail systemic thrombolysis, catheter-directed clot extraction procedures or surgical embolectomy are appropriate options.

Bleeding – Bleeding rates vary among studies. In general, rates of major bleeding range from 10 to 20 percent for systemic agents, while lower rates in the region of 4 percent or less have been reported for CDT. Similarly, approximately 2 to 5 percent may experience intracranial hemorrhage with systemic agents, while rates of <1 percent are reported in those who receive CDT.

The only FDA-approved indication for PE fibrinolysis is massive PE. For patients with preserved systolic blood pressure and submassive PE with moderate or severe RV dysfunction, ACCP guidelines for fibrinolysis recommend individual patient risk assessment of the thrombotic burden versus the bleeding risk.

Catheter-Directed Treatment:

Involves the insertion of a catheter into the pulmonary arteries, which is then used for ultrasound-assisted thrombolysis, suction embolectomy, rotational embolectomy, thrombus aspiration, or combining mechanical fragmentation with pharmacological catheter-directed thrombolysis. Different studies have shown a success rate of up to 87% for catheter-directed therapies. Catheter-assisted embolectomy techniques carry the inherent risk of perforating the pulmonary arteries, leading to massive hemoptysis or cardiac tamponade. These complications are rare but fatal.

The first, catheter-directed thrombolytics, involves local delivery of lytic therapy to the pulmonary arteries. This may be performed using a standard pigtail catheter or pulmonary artery catheter to deliver the lytics locally. Alternatively, the lytics may be delivered using the EKOS EkoSonic (BTG PLC; London, UK) catheter for ultrasound-assisted catheter-directed thrombolysis. This catheter uses locally delivered ultrasound to separate fibrin strands in the thrombus, potentially enhancing penetration of the thromolytic. The second catheter-directed approach includes mechanical thrombectomy, which may be used in isolation or in combination with lytic therapy based on the clinical scenario. The catheter systems currently approved for this indication include the Penumbra Indigo (Penumbra, Inc.; Alameda, CA) and FlowTriever (Inari Medical, Inc.; Irvine, CA) catheters.

Surgical Embolectomy:

It is usually indicated in a patient with hemodynamically unstable PE in whom thrombolysis (systemic or catheter-directed) is contraindicated, or in patients who have failed

thrombolysis. The risk of intracranial hemorrhage with fibrinolysis has prompted a renaissance of surgical embolectomy. More prompt referral before the onset of irreversible cardiogenic shock and multisystem organ failure and improved surgical technique have resulted in a high survival rate.

Differential Diagnosis:

Since pulmonary embolism has a very heterogeneous clinical presentation ranging from dyspnea to sudden cardiac arrest. The differential diagnosis of PE is extensive and includes:

- Acute coronary syndrome
- Stable angina
- Acute pericarditis
- Congestive heart failure
- Malignancy
- Cardiac arrhythmias
- Pneumonia
- Pneumonitis
- Pneumothorax
- Vasovagal syncope

Enhancing Healthcare Team Outcomes

Some hospitals are establishing multidisciplinary pulmonary embolism response teams (PERTs) to facilitate prompt diagnosis and timely treatment of patients with pulmonary embolism. A PERT is a treatment model composed of providers from different specialties involved in the treatment of PE, including pulmonary, critical care, cardiology, and cardiothoracic surgery, among others. The establishment of PERT has proven effective in multiple studies by improving communication and coordinating treatment efforts among providers

Conclusions

PE is a common clinical problem with varied manifestations ranging from benign to fatal. Given the complexities of diagnostic, stabilization, and treatment modalities, a rapidly assembled and collaborative multi-disciplinary approach is helpful.



Fig 2: CTPA demonstrating saddle pulmonary embolism partially obstructing both main pulmonary arteries; the white area above the center is the pulmonary artery, opacified by radiocontrast; the black arrow indicates the pulmonary thrombus.

References:

- (i) Thompson, T., & Kabrhel, C. (2022). Overview of acute pulmonary embolism in adults. UpToDate https://www.uptodate.com/contents/overview-of-acute-pulmonary-embolism-in-adults?search=pulmonary%20embolism&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
- (ii) Goldhaber, S. Z. (2012). Deep Venous Thrombosis and Pulmonary Thromboembolism. pp 2170-77 Harrison's Principles of Internal Medicine 18th Ed The McGraw-Hill Companies, Inc.
- (iii) Myotonic dystrophy type 1 and pulmonary embolism: Successful thrombus resolution with dabigatran etexilate therapy - Scientific Figure on ResearchGate. Available from: <https://www.researchgate.net/figure/> Computed-thomography-pulmonary-angiography-CTPA-demonstrating-saddle-pulmonary-embolism_fig2_331560093 [accessed 31 Oct, 2022]
- (iv) Vyas V, Goyal A. Acute Pulmonary Embolism. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK560551/>
- (v) Alejandra Gutierrez Bernal, ; Christina Fanola, ; Jason Alan Bartos, Management of PE <https://www.acc.org/latest-in-cardiology/articles/2020/01/27/07/42/management-of-pe>
- (vi) Freund Y, Cohen-Aubart F, Bloom B. Acute Pulmonary Embolism: A Review. JAMA. 2022; 328(13):1336–1345. doi:10.1001/jama.2022.16815



Haemoptysis- A Serious Medical Emergency

Dr Surya Kant

Professor & Head

Department of Respiratory Medicine, KGMU, UP, Lucknow

National Vice Chairman, IMA-AMS

Introduction

Haemoptysis is the expectoration of blood that originates from the lower respiratory tract. [1] Bleeding from the upper airways is excluded from this definition. Massive hemoptysis is a potentially life-threatening emergency and requires rapid diagnosis and treatment. Although over 90% of haemoptysis are self-limiting, both the diagnosis and the treatment of massive haemoptysis are challenging.

True haemoptysis, with the source of bleeding in the airways or lungs, must be distinguished from pseudo-haemoptysis, where the blood originates from the upper gastrointestinal tract or the upper respiratory tract (mouth, nose, or throat). Pseudo-haemoptysis occurs due to infections with *Serratia marcescens*, which produces a red pigment. So, there is red expectoration, but there are no RBCs in the sputum. False haemoptysis /spurious haemoptysis is bleeding from the upper aerodigestive tract (gums, nose or pharynx). The vast majority of cases of haemoptysis occur in adults (mean age 62 years, male:female ratio 2:1 ; only rarely are children affected.[2]

Severity of Haemoptysis

Haemoptysis is usually a self-limiting event but in fewer than 5% of cases, it may be massive. Haemoptysis is mainly classified by the amount of blood expectorated into mild, moderate and massive. Massive haemoptysis is either e"500 ml of expectorated blood over a 24 hour period or bleeding at a rate e"100 mL/hour. A large volume of expectorated blood alone does not define massive haemoptysis, rather an amount of blood sufficient to threaten the patient's life can be a

more correct and functional definition of severe haemoptysis. Massive haemoptysis is usually a life threatening condition with mortality rate of more than 50%. Flooding of the airways with blood leads to asphyxiation, and this is usually the cause of death rather than exsanguination.[3]

Haemoptysis should be differentiated from hematemesis as shown in following Table.[4]

Etiology:

Two arterial vascular systems supply blood to the lungs: the pulmonary arteries and the bronchial arteries. The pulmonary arteries provide 99% of the arterial blood to the lungs and are involved in gas exchange. The bronchial arteries supply nourishment to the extra- and intrapulmonary airways. The bronchial arteries are direct branches of aorta, hence blood flow is at systemic pressure, while pulmonary arteries have 1/3rd systemic pressure. In cases of severe hemoptysis, the source of bleeding usually originates from bronchial vessels (in 90% cases) and pulmonary arteries in 5% cases.[5]

The following are the common causes that are to be searched for in a case of hemoptysis.[6]

Anatomy and Pathophysiology

The lungs receive blood from two sources: the pulmonary arteries, which are responsible for gas exchange, and the remaining capillaries. 1% is derived from the bronchial arteries. [9] Bronchial arteries run parallel to the bronchi and branch off to supply the trachea, bronchi (peribronchial plexus), and the vasa vasorum of the pulmonary vessels. Bronchopulmonary anastomoses connect the bronchial arteries to the pulmonary arteries.

Table 1: Differentiation of haemoptysis from hematemesis:

Haemoptysis	Hematemesis
1. There is usually a tingling sensation in the throat prior to the episode.	Patient will usually complain of nausea and upset stomach
2. The blood is frothy and bright red.	Blood is dark red, brown and non-frothy.
3. Blood is associated with mucus.	Blood is associated with food particles.
4. pH will be neutral to alkaline	Blood will give an acidic pH.
5. Stool examination for occult blood is usually negative.	Stool is almost always positive for occult blood.
6. There is history of lung disease.	There is history of liver disease.
7. Not associated with malena.	Associated with malena.
8. Patient is usually a smoker.	Patient is usually an alcoholic.
9. Asphyxia is possible and common.	Asphyxia is unusual.

Table 2: Etiology of haemoptysis

Infections	Pulmonary tuberculosis Post tuberculosis Rasmussen's Aneurysm PneumoniaLung abscess Bronchiectasis Fungal infections[7] Hydatid cyst[8]
Neoplasms	Bronchogenic carcinoma Metastatic nodules Carcinoid tumor Bronchial adenoma Hamartoma
Cardiovascular disorders	Mitral stenosis Pulmonary infarction from thromboembolism
Trauma	Penetrating lung injuryLung contusion
Hematologic disorders	Blood dyscrasias
Auto-immune disorders	Goodpasture's syndrome Wegener's Granulomatosis Small and medium vessel vasculitis
Metabolic Disorders	UremiaLiver cirrhosis
Vascular Disorders	Pulmonary arterio-venous malformation (PAVM) Osler Weber rendu syndrome Takayasu arteritis
Drug-induced	Anti-platelet drugs Anti-coagulant drugs NSAIDs D- penicillamine

The blood is drained venous from the bronchial arteries primarily through the bronchial veins into the right atrium, but also through the pulmonary veins into the left atrium.

When the pulmonary arterial circulation is compromised, the secretion of neoangiogenic growth factors leads to bronchial artery proliferation.[10]

Such impairments can be caused by the following

- 1) Hypoxia-induced vasoconstriction
- 2) Thrombosis or pulmonary arterial thromboembolism
- 3) Vasculitis is a type of autoimmune disease.
- 4) Chronic inflammatory or malignant lung disease
- 5) Pulmonary arterio-venous fistula (e.g., Osler disease).

Because of the thinner, more fragile bronchial artery walls, the systemic arterial pressure load, and the opening of the arteries into chronically inflamed zones or neoplasms, airway ruptures and haemorrhages occur, manifesting clinically as haemoptysis .Angiographic and bronchoscopic studies, as well as measurements of expectorated blood oxygenation, have revealed that approximately 90% of hemoptysis originate in the bronchial arteries, 5% in the pulmonary arteries, and 5% in non-bronchial systemic arteries .[11]

Approach to patient:

History:

The history should be directed towards the cause that is relevant to the setting as treatment is mainly treating the primary cause. The color, amount of blood and associated symptoms should be asked to determine the cause of hemoptysis and to differentiate from upper gastro-intestinal (GI) bleed or bleeding from nasal tract. Old age and smoking should warrant search for malignancy. Constitutional symptoms such as fever, fatigue, malaise and expectoration are usually seen in

infectious causes. Recurrent childhood infections, recurrent sinusitis, infertility can be associated with bronchiectasis or cystic fibrosis.[12] Foul smelling copious expectoration with postural variation is usually seen in lung abscess. Joint pains, skin lesions, epistaxis, hematuria and a family history might be a clue to auto-immune disorders. Bronchogenic carcinoma might be associated with hoarseness of voice, superior vena cava obstruction, loss of weight and appetite. Sudden onset chest pain and dyspnea can be a feature of pulmonary thrombo-embolism.

EXAMINATION:

Physical examination:

Severity of anemia has to be assessed. Clubbing may be a feature of bronchiectasis, cystic fibrosis, lung abscess and PAVM. Oral and nasal cavity should be examined to find alternate sources of bleeding. Pedal edema might give a clue towards cardiovascular cause. The patient might have tachypnea, tachycardia, use of accessory muscles, cyanosis, fatigue, and diaphoresis indicating any respiratory or cardiac cause. Features of SVC obstruction are seen in malignancy and nasal septal deformity is associated with Wegener's granulomatosis.

Respiratory system:

Auscultation of lungs plays an important role in localizing lesions. Findings that should be kept in mind are focal wheeze and crepitations.

Other system examination:

Auscultation of heart will be helpful in finding murmur of mitral stenosis or mitral regurgitation which are important causes of haemoptysis. Examination of skin helps in identifying bruising-potentially suggestive of coagulopathy, telangiectasia of Osler-Weber-Rendu, palpable purpura or other rash suggestive of vasculitis.

INVESTIGATIONS: Following investigations are helpful in reaching the final diagnosis. [13]

Biochemical tests:

Hemoglobin and blood counts- Hemoglobin levels

can be low due to hemoptysis which should be corrected either orally or parenterally depending on the degree of anemia. Leukocyte count is an important indicator of infection in conditions like pneumonia, lung abscess and bronchiectasis.

Renal function tests- Deranged urea and creatinine levels indicate conditions like Good pasture syndrome, Wegener's granulomatosis and uremia. Urine microscopic examination might give clues to diagnose occult bleeding in urinary tract and renal conditions such as vasculitis that may be a primary cause of hemoptysis.

Bleeding profile- Prothrombin time/International normalized ratio (PT/INR), Bleeding time and clotting time should be done to detect intrinsic clotting defects. Deranged coagulation profile due to any cause can lead to hemoptysis. They include Immune thrombocytopenic purpura (ITP), Disseminated intravascular coagulation (DIC), drug use like anti platelets and warfarin.

Bacteriologic :

Sputum examination for acid fast bacilli, Gram stain and fungal elements, along with culture should be done in suspected infective cases.

IMAGING: Following radiological investigations are of great help in differentiating etiology of Hemoptysis. [14]

Chest x-ray (CXR)

It is considered the initial imaging modality for evaluating patients with hemoptysis. It is quick, inexpensive, and readily available. CXR can assist in lateralizing bleeding and reveal a focal or diffuse lung involvement. CXR may detect underlying parenchymal and pleural abnormalities such as mass, pneumonia, chronic lung disease, atelectasis, cavitary lesion, and alveolar opacities due to alveolar hemorrhage.

Contrast enhanced computed tomography (CECT) thorax:

Since sensitivity of chest x ray is not very high and all causes of hemoptysis cannot be delineated by CXR, it is essential to get a CECT thorax in certain

sub group of patients. It represents a noninvasive and highly useful imaging tool in the clinical context of hemoptysis and allows a comprehensive evaluation of the lung parenchyma, airways, and thoracic vessels by using contrast material.⁴ CT may identify the bleeding site in 63% to 100% of patients with hemoptysis and has the ability to uncover the potential underlying causes of bleeding, such as bronchiectasis, pulmonary infections and lung cancer⁵.

CT Pulmonary angiography:

CT pulmonary angiography is important to identify origin and course of arteries causing the bleeding. Pulmonary hemorrhage usually appears as focal or diffuse hazy consolidation or ground-glass opacity, even though thickened interlobular septa superimposed on a background of ground-glass attenuation ("crazy paving" pattern) have also been described.

BRONCHOSCOPY:

For many years bronchoscopy has been considered the primary method for diagnosing and localizing hemoptysis, especially if massive. Bronchoscopy, performed with either a rigid or flexible endoscope, is helpful in identifying active bleeding and for assessment of the airways in patients with massive hemoptysis. Bronchoscopy yields additional information about endobronchial lesions, mucosal abnormality, site for biopsy and allows samples for tissue diagnosis, microbial cultures, broncho-alveolar lavage (BAL) fluid for cell counts, cultures and brush smears. Moreover, with bronchoscopy, cold saline solution can be instilled directly into the airways at the level of the bleeding source, if identified, and balloon inflation or laser coagulation may be used to control hemorrhage.

RHEUMATOLOGIC:

Peri-nuclear Anti Neutrophilic Cytoplasmic Antibody (p-ANCA), Cytoplasmic Anti Neutrophilic Cytoplasmic Antibody (c-ANCA), Rheumatoid factor (RA), Anti-cyclic Citrullinated Peptide (anti-CCP) are important indicators for immune

mediated diseases like vasculitis and rheumatologic disorders. [15]

MANAGEMENT:

Historical perspective:

In olden days, pneumoperitoneum was created artificially by injecting air into the peritoneal cavity. This led to elevation of diaphragm and compression of lung segments, causing suppression of bleeding by tamponade action over affected vessels. But, with development of newer, more effective modalities of treatment and due to lack of familiarity with this procedure, it is no longer practised and only has a historical significance.

Management of massive hemoptysis :

Primary management:

Management of massive hemoptysis is always an emergency.² Maintenance of airway is the primary management. Oxygen saturation should be checked and oxygen supplementation must be given. Patients with massive hemoptysis should be immediately placed into a position in which the presumed bleeding lung is in the dependent

position to protect the healthy lung. Patients with massive hemoptysis are typically tachycardic and may become hypotensive. Such patients should be managed with volume resuscitation. Crystalloid intravenous fluids are generally administered first. However, blood products are an appropriate alternative in patients who are coagulopathic, anemic, and/or bleeding rapidly. Patients with massive hemoptysis may also have arrhythmias that are probably a consequence of respiratory distress and hypoxemia. [16]

Management of cause:

Bronchoscopy:

In patients with massive hemoptysis, after initial stabilisation of the patient, bronchoscopy should be done to detect the site of bleeding and perform interventions. The various therapeutic options are balloon tamponade, cold saline lavage, topical agents like epinephrine, vasopressin, laser therapy and electrocautery.

Surgical management:

Patients with unilateral, uncontrollable bleeding should be evaluated by a thoracic surgeon early. Surgical management is useful in cases where

Table 3:Initial Assessment of haemoptysis

Action	Purpose
Monitor the vital parameters	Registration of pulse-oximetric oxygen saturation (SpO ₂), respiratory and circulatory function (non-invasive blood pressure measurement [NIBP]); assessment of risk involved in interventional procedures and medicinal treatment
Give oxygen	Improvement of oxygenation
Place the patient with the bleeding side down	Prevention of the flow of endobronchial blood into unaffected lung segments
Sedation/anxiolytics	Calming of the patient, facilitation of diagnostic and therapeutic measures (NB: re - striction of breathing activity, ability to expectorate, ability to cooperate/communicate)
In massive hemoptysis: endotracheal or, if required, unilateral endobronchial intubation	Maintenance of gas exchange

bronchoscopy fails. Typical diseases where thoracic surgery plays a role include bronchiectasis, aspergilloma and healed tubercular lesions. The various surgeries include surgical lung resection through lobectomy and pneumonectomy. However morbidity and mortality associated with surgical management is high.

Until the 1980s, the primary treatment for hemoptysis was surgery, which had a mortality rate of 37 to 42% in the emergency scenario and 7 to 18% in the interval between bleeding events. Recurrent hemoptysis is treated with lobectomy and pneumonectomy. It is not used when the lung parenchyma is diffusely involved; rather, a localised lesion is an indication for surgical intervention. [17]

Bronchial Artery Embolization (BAE):

Bronchial artery embolization is a safe and effective non surgical treatment for patients with massive hemoptysis. BAE has been extensively used in the management of hemoptysis in patients with aspergilloma. However, this approach has proved to be only temporarily effective, and recurrence of hemoptysis usually occurs because of the presence of collateral vessels in the involved area. Hence, BAE seems to be appropriate only as a "bridge" procedure in patients with massive hemoptysis until surgical resection. [18]

Management of mild-moderate hemoptysis:

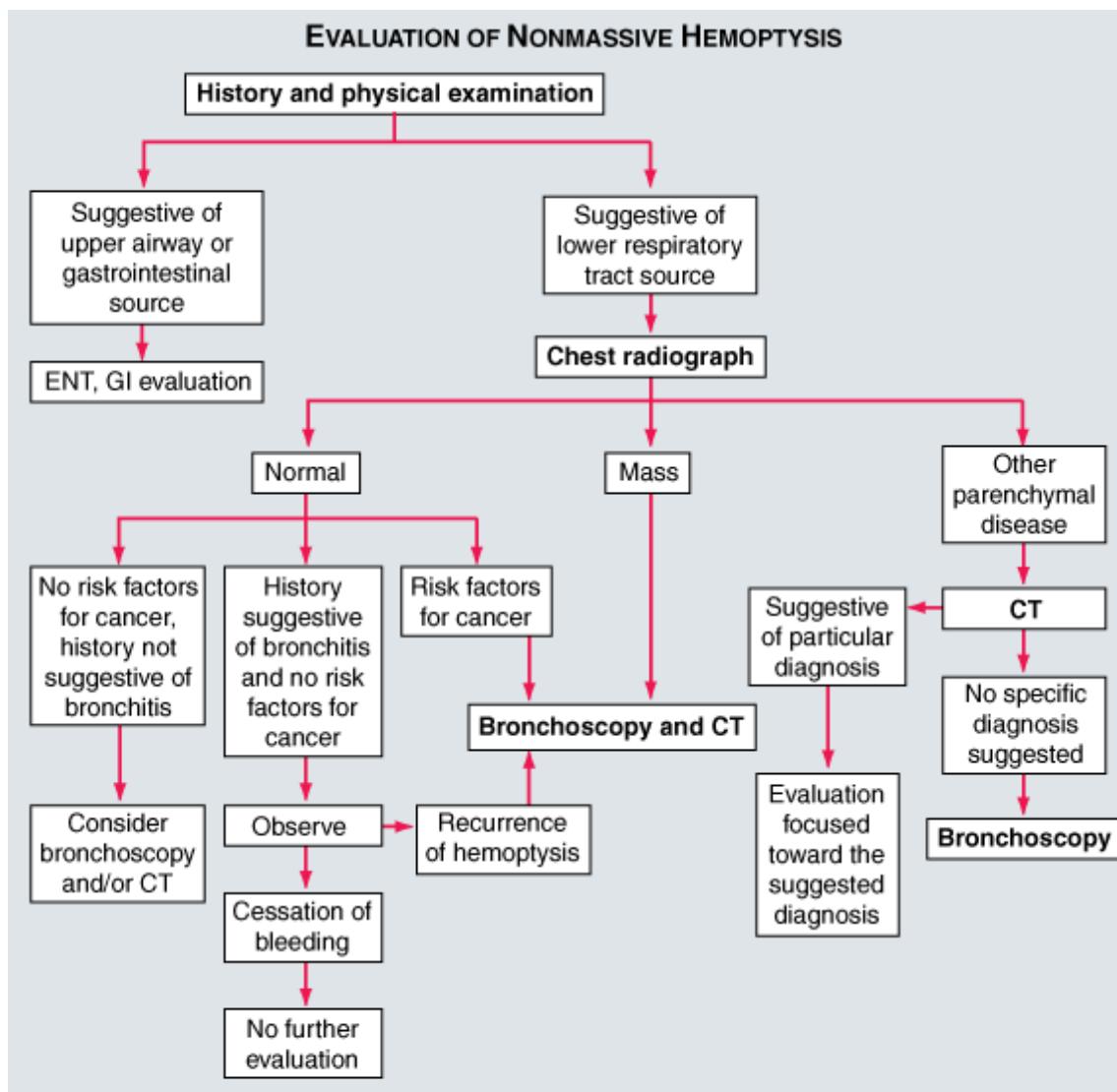
All patients having hemoptysis should be advised complete bed rest. The diseased side should be kept in a dependent position while lying down so that the affected blood vessels are compressed due to gravity. Measures should be taken to suppress cough as it produces undue strain over these vessels. The commonly used cough suppressants include dextromethorphan (central cough suppression) and levocloperastine (peripheral cough suppression) and Codeine containing preparations.[19] Hemostatic agents should be given as primary management. Tranexamic acid is an anti-fibrinolytic drug which prevents plasmin from binding to and degrading fibrin. Ethamsylate is a hemostatic agent which increases capillary endothelial resistance and

promotes platelet adhesion. Botropase is an aqueous solution of enzyme hemocoagulase (derived from venom of a species of pit viper) and acts as a hemostatic drug reserved for patients with massive hemoptysis.[20] Prophylactic antibiotics should be given to all patients with hemoptysis as blood is a good culture media. Anxiolytics are also prescribed to relieve anxiety and stress associated with hemoptysis. In addition to these general measures, adequate treatment of the primary cause should be undertaken.

CONCLUSION:

The following recommendations are the result of evidence-based consensus by the American College of Radiology Appropriateness Criteria Expert Panel on Thoracic Radiology:¹

- (1) Initial evaluation of patients with hemoptysis should include a chest radiograph;
- (2) Patients at high risk for malignancy (>40 y old, >40 pack-year smoking history) with negative chest radiograph, computed tomography (CT) scan, and bronchoscopy can be followed with observation for the following 3 years. Radiography and CT are recommended imaging modalities for follow-up. Bronchoscopy may complement imaging during the period of observation.
- (3) In patients who are at high risk for malignancy and have suspicious chest radiograph findings, CT is suggested for initial evaluation; CT should also be considered in patients who are active or exsmokers, despite a negative chest radiograph; and
- (4) Massive hemoptysis can be effectively treated with either surgery or percutaneous embolization. Contrast-enhanced multidetector CT before embolization or surgery can define the source of hemoptysis as bronchial systemic, nonbronchial systemic, and/or pulmonary arterial. Percutaneous embolization may be used initially to halt the hemorrhage before definitive surgery. Hemoptysis is a life



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>

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Figure 1 Evaluation of non massive hemoptysis

threatening condition which can be the presenting complaint in a large number of respiratory as well as systemic disorders. If the cause of hemoptysis is diagnosed in time and aggressively managed, the patient's life can be saved.

REFERENCES:

1. Jeudy J, Khan AR, Mohammed TL, et al. ACR Appropriateness Criteria hemoptysis. *J Thorac Imaging* 2010; 25:W67"69.
2. Lordan JL, Gascoigne A, Corris PA. The pulmonary physician in critical care Illustrative case 7: Assessment and management of massive haemoptysis. *Thorax* 2003; 58:814–819.
3. Ibrahim, WH. Massive haemoptysis: the definition should be revised. *Eur Respir J* 2008; 32:1131.
4. Hirshberg B, Biran I, Glazer M, et al. Hemoptysis: etiology, evaluation, and outcome in a tertiary referral hospital. *Chest* 1997;112:440-4.

5. Reisz G, Stevens D, Boutwell C, et al. The causes of hemoptysis revisited. A review of the etiologies of hemoptysis between 1986 and 1995. Missouri Medicine 1997;94:633-5.
6. Bruzzi JF, Remy-Jardin M, Delhaye D, Teisseire A, Khalil C, Remy J. Multi-detector row CT of hemoptysis. Radiographics 2006; 26:3-22.
7. S Kant*, SMehra An interesting case of haemoptysis.The Int J of Pulmonary Medicine.2007;9(1)
8. S Kant, S Verma. Fungal ball presenting as "Haemoptysis". The Int J of Pulmonary Medicine. 2008;10(1):1-4
9. Chamilos G, Kontoyannis D.P. Aspergillus, Candida and opportunistic mold infections of the lung. Fishman's pulmonary diseases and disorders. 4th Ed, 2008. Mc Graw Hill: 2291-2304.
10. Chun JY, Morgan R, Belli AM. Radiological management of hemoptysis: a comprehensive review of diagnostic imaging and bronchial arterial embolization. *Cardiovasc Intervent Radiol.* 2010;33:240-250.
11. Surya Kant, Sanjay Singhal and S.K. Verma. Allergic bronchopulmonary aspergillosis presenting as haemoptysis: A case report. June 2006. *Journal of Internal Medicine of India* 9(2):62-64
12. Jean-Baptiste E. Clinical assessment and management of massive hemoptysis. *Critical care medicine.* 2000 May 1;28(5):1642-7.
13. Hsiao EI, Kirsch CM, Kagawa FT, Wehner JH, Jensen WA, Baxter RB. Utility of fiberoptic bronchoscopy before bronchial artery embolization for massive hemoptysis. *AJR Am J Roentgenol* 2001; 177:861-867.
14. Roebuck DJ, Barnacle AM. Haemoptysis and bronchial artery embolization in children. *Paediatric respiratory reviews.* 2008 Jun 1;9(2):95-104.
15. Yoon W, Kim JK, Kim YH, Chung TW, Kang HK. Bronchial and nonbronchial systemic artery embolization for life-threatening hemoptysis: a comprehensive review. *Radiographics.* 2002 Nov;22(6):1395-409.
16. Deffebach ME, Charan NB, Lakshminarayan S, Butler J. The bronchial circulation: small, but a vital attribute of the lung. *American Review of Respiratory Disease.* 1987 Feb;135(2):463-81. Earwood JS, Thompson TD. Hemoptysis: evaluation and management. *American family physician.* 2015 Feb 15;91(4):243-9
17. Kant S, Bajpai J, Bajaj DK, Pathak R, Rajagopal TV. Pulmonary hydatid cyst presenting with hemoptysis. *Ind J Imm Res Med* 2017;2(2):58-59
18. Bajpai J, Bajaj DK, Kushwaha RA, Kant S, Pradhan A, Verma AK, et al. A rare cause of hemoptysis in a young female. *J Med Sci* 2022;42:42-5
19. Fartoukh M, Khoshnood B, Parrot A, et al. Early prediction of in-hospital mortality of patients with hemoptysis: an approach to defining severe hemoptysis. *Respiration* 2012;83:106-14.
20. Surya Kant. Clinical approach to hemoptysis. In *Clinical methods in respiratory medicine.* Jaypee Brothers Medical Publishers (P) Ltd; 2018: 45-53.



Endocrine Emergencies

Dr V. Sri Nagesh

Adult & Pediatric Endocrinologist & Diabetologist
Sri Nagesh Diabetes Thyroid & Endocrine Clinic, Hyderabad

Among all the emergencies encountered by the general practitioner, the physician or the intensive care specialist in daily clinical practice, the least amount of significance is most often given to endocrine emergencies due to a few significant reasons – (a) their perceived rarity (b) the often mistaken assumption that they are not life threatening (c) lack of familiarity of treating doctors with endocrine disorders and their endocrine manifestations (d) scarcity of endocrinologists even at tertiary care centres (which is now rapidly changing) and at times, unwillingness to involve endocrinologists in management of disorders that are often misconstrued as simple medical emergencies that do not require specialised referrals and can be managed a primary or secondary care settings (e) the need for accurate hormone lab investigations which are often unavailable at primary care level and not always available even at tertiary care level and last but not the least, (f) the insidious nature of endocrine emergencies and the fact that an emergency presentation is often the first manifestation of an endocrine disorder –especially true of Type 1 diabetes, adrenal insufficiency hypoparathyroidism and pheochromocytoma

The lion's share of presentations, resources and clinical contact in endocrine emergencies is always claimed by diabetic ketoacidosis and hypoglycemia, but there are other emergencies, albeit less common, that command attention of the clinician to prevent morbidity and mortality in the emergency setting. This article will focus primarily on the etiology, presentation, pointers to diagnosis, rapid diagnostic tests –especially at the primary care setting, emergency management and need for referral and further follow-up –for reasons of simplicity and brevity.

1. Myxedema Coma

Myxedema coma is a rare life-threatening emergency in patients with chronic untreated hypothyroidism where precipitating events like an infection, use of diuretics or bleeding diatheses overwhelm the adaptive mechanisms that maintain homeostasis. Classical myxedema coma is characterized by a triad of coma or altered sensorium, hypothermia and presence of a precipitating event in the setting of hypothyroidism.

On examination most patients are lethargic or comatose, even though coma is not always mandatory, cold to touch, hypoxic with reduced respiratory drive and saturations, dry coarse skin, bradycardia, pedal edema and markedly delayed deep tendon reflexes.

Lab testing reveals severe anemia, hyponatremia, elevated LDL and triglycerides, low T3 and T4 and very high TSH (though TSH maybe normal in central hypothyroidism or non-thyroidal illness syndrome), elevated liver enzymes and elevated LDH and creatine kinase. A baseline ECG prior to initiation of treatment is important as thyroid replacement can precipitate an acute coronary syndrome as is a 2D echo to diagnose a pericardial effusion.

Management

In critical care setting, emphasis is on treatment of hypoventilation, hypothermia, electrolyte and cardiac abnormalities. Use of oxygen and ventilators is needed as appropriate. Careful volume resuscitation with normal saline along with management of hyponatremia and hypoglycemia is recommended. Inotropes and glucocorticoids should be given under the cover of antibiotics

when required. External warming should be attempted with blankets but too vigorous warming should be avoided for fear of peripheral vasodilatation and heat loss.

Definitive treatment remains administration of thyroid hormones. A controversy of T4 alone versus T3 +T4 exists. A rational approach would involve a fairly large initial iv dose of 300-500 µg T4 and if there is no response addition of 10-25 mcg T3. Lower doses should be administered in elderly patients, leaner patients, or patients with history of coronary artery disease or arrhythmia. In the setting of severe hyponatremia (105–120 mmol/L), 3% sodium chloride can be given, but never correct sodium more than 10–12 mmol/L in 24 h or 18 mmol/L in 48 h to avoid precipitating osmotic demyelination syndrome (ODS).

The mortality can be upto 25% in myxedema coma with advanced age, comatose state, infections and higher SOFA score being cited as poorer prognostic factors. It should be noted that though rare, it is a very serious emergency and needs to be referred and managed appropriately in an ICU setting, ideally including a team comprising of an endocrinologist, cardiologist, critical care specialist and pulmonologist.

2. Thyroid Storm

Thyroid (or thyrotoxic) storm is an acute, life-threatening emergency that has now become infrequent due to better and earlier detection of thyrotoxicosis and management. However, precipitating factors like infection, surgery, radio-iodine therapy or use of iodinated contrast can precipitate thyroid storm in a person who is known to have hyperthyroidism or is hitherto unknown to have this disorder. (TABLE 1)

Presenting features

Most patients present with high fever (temperature often exceeding 105 degrees F), severe tachycardia (>130 bpm), arrhythmias, dehydration, confusion, psychosis, jaundice and hepatic dysfunction, diarrhea and vomiting. A detailed history will almost always elicit one of the precipitating factors mentioned in Table 1, sudden withdrawal of anti-thyroid drugs being the most common. Butch Warthofsky Point Scale and Japanese Thyroid

Association classification system can be used for diagnosing thyroid storm, though the disorder is often self-evident with a well elicited clinical history or if signs like a large goiter, exophthalmos or tachyarrhythmias are apparent.

Increased availability of intracellular free thyroid hormone, elevated oxygen demand, enhanced adrenergic drive are responsible for the changes seen in thyroid storm. Diagnosis of thyroid storm is made on clinical grounds. T4 levels are elevated and TSH levels are suppressed. Free T3 in preference to T3 should be measured in view of non-thyroidal illness syndrome.

Treatment

Treatment requires admission to an intensive care unit and comprises of supportive care, primary therapy and second line management. Supportive care includes oxygen, cooling, fluid and electrolyte maintenance, cardiac support, nutritional care and sedation.

Definitive therapy involves counteracting the effects of thyroid hormones. This includes the use of beta blockers either propranolol 60-80 mg oral every 4 hours or initial dose of 0.5–1.0 mg mg iv every 6 hours, gradually increasing upto 1-3 mg every 6 hours. In the ICU setting, esmolol iv can also be used at loading dose of 250 mcg/kg to 500 mcg/kg followed by 50 mcg/kg to 100 mcg/kg/minute. These essentially help to counter the peripheral adrenergic effects of thyroid hormone.

Definitive therapy involves use of anti-thyroid drugs –either PTU or methimazole or carbimazole. PTU has the advantage over methimazole (MMI) of decreasing the conversion of T4 to T3. Because of this unique property, thyroid storm remains one of the few conditions in which PTU is used preferentially over the more potent MMI. PTU and MMI are generally given orally or per nasogastric tube as required since parenteral preparations are not available. PTU should be given as a dose of 600–1000 mg and then given at doses of 200–250 mg, fourth hourly doses. MMI is given at a total daily dose of 120 mg in divided doses of 20 mg every 4 hours.

Antithyroid drug therapy, although highly effective at inhibiting new hormone synthesis, has little

impact on release of preformed thyroid hormone, a role which is therefore relegated to inorganic iodine therapy.

Inorganic iodine directly inhibits colloid proteolysis, release of T4 and T3 from the thyroid gland, and inhibits thyroid hormone synthesis, through the Wolff-Chaikoff effect. Recommended oral doses are either Lugol's solution (8 mg/drop [0.05 ml]) 8 drops every 6 h, or saturated solution of potassium iodide (SSKI) (< "35–50 mg/drop) 5 drops every 6 h. These solutions are not widely available and need to be prepared as per standard pharmacopeia.

Oral cholecystographic contrast agents such as ipodate and iopanoate, by virtue of a large content of stable iodine (308 mg/500 mg capsule for ipodate) have actions similar to inorganic iodide. They are also potent inhibitors of peripheral conversion of T4-to-T3. Ipodate is given at a daily dose of 1–3 gm and, like iodides, should be preceded by prior blockade of new thyroid hormone synthesis with PTU or MMI.

As a last resort, cholestyramine to remove thyroid hormones from enterohepatic circulation, plasmapheresis and charcoal plasmapherfusion have been used for the physical removal of circulating hormone, especially those patients who do not respond well to conventional therapy, patients with agranulocytosis or hepatic dysfunction. It should be noted that these are temporary measures and may need to be repeated till the more conventional methods become effective.

Glucocorticoids like (2 mg dexamethasone every 6 h) depress serum T3 levels by reducing T4 to T3 conversion. This effect of glucocorticoids is beneficial in thyroid storm and can be used in this clinical setting.

Permanent management of the thyrotoxicosis by either 131-I or thyroidectomy should be deferred until euthyroidism is restored.

3. Hypocalcemia

Hypocalcemia is a common electrolyte disturbance complicating approximately 15–30% of hospital admissions, and up to 90% of critically

ill patients admitted to an intensive care unit (ICU) can exhibit some amount of hypocalcemia. A brief etiology of hypocalcemia is mentioned in Table 2. Hypocalcemia can either be chronic or acute. This can determine the severity of hypocalcemia and prognosis of patient.

Diagnostic Testing

This includes measurement of total or ionized calcium, albumin, serum phosphorus, PTH, creatinine, and 25 hydroxyvitamin D and serum magnesium levels. Additional testing maybe required for causes mentioned in Table 2 as per etiology. The ECG hallmark of hypocalcemia is prolongation of the corrected QT interval (QTc), the duration of which is proportional to the degree of hypocalcemia.

Treatment

Patients with severe hypocalcemia, usually <7.5 mg/dl, or with neurological manifestations or stridor (laryngo/bronchospasm) should receive intravenous calcium. 10-20 ml (90–180 mg elemental calcium) 10% calcium gluconate should be infused slowly in 50–100 ml 0.9% saline (or 5% dextrose) over 10–20 minutes (with cardiac monitoring). A chronic intravenous drip is then started if the patient is still symptomatic and oral treatment cannot act rapidly enough. The infusion rate should be guided by signs, symptoms, and calcium measurements checked every 1-2 hours, preferably ionized calcium levels. Magnesium deficiency should also be treated when present, since it can attenuate the effect of the treatment by calcium and vitamin D. Oral calcium (e.g., 1-2 grams of elemental calcium) and a rapidly acting preparation of vitamin D (e.g., 0.5-1.0 micrograms of calcitriol in divided doses) should be started as soon as oral treatment is feasible intravenous calcium should be continued until oral therapy has taken effect. Patients taking cardiac drugs, especially digoxin, are predisposed to cardiotoxicity by infusion of calcium, so an ECG should be used for cardiac monitoring. There is limited data on the use of recombinant PTH in human subjects who are acutely hypocalcemic.

4. Pituitary Apoplexy

Pituitary apoplexy (PA) is a rare syndrome due to

abrupt hemorrhage and/or infarction of the pituitary gland, generally within a pituitary adenoma. Its prevalence is about 6.2 cases per 100000 people. PA can occur at all ages but is most frequent in the fifth or sixth decade of life with a slight male preponderance. While all large pituitary tumors are at risk for hemorrhagic infarction, functional pituitary tumors like Cushing's disease or acromegaly may be particularly prone, especially in the setting of inadequately treated hypertension.

Symptoms

Apoplexy presents with the characteristic triad of headache, vomiting and visual disturbances. Headache is often the initial symptom, with sudden and severe onset described "like a thunderclap. It is often retroorbital but can be diffuse also. It is associated with nausea and vomiting. Visual disturbances and oculomotor palsies , especially of the 3rd cranial nerve can be described. Acute endocrine dysfunction may also be present, with corticotroph deficiency being the commonest occurrence.

Imaging is the cornerstone of diagnosis with MRI being the modality of choice. MRI can identify hemorrhagic and necrotic areas and show the relationship between the tumor and neighboring structures such as the optic chiasm,cavernous sinuses, and hypothalamus. MRI T2 weighted images are the test of choice and should be performed emergently in all patients with visual symptoms. A CT scan can be useful when an MRI is neither available or possible.

Serum electrolytes, renal and liver function, complete blood count with platelets, and prothrombin time can be useful. Measurement of free T4, TSH, prolactin, ACTH and serum cortisol are always helpful. Differential diagnoses include sub arachnoid hemorrhage, migraine, infectious meningitis, cavernous sinus thrombosis and CVA.

Treatment

Successful management of pituitary apoplexy needs a team of critical care specialists, neurologists, neurosurgeons, ophthalmologist and endocrinologists. Acute secondary adrenal insufficiency is the major source of mortality

associated with this condition and early glucocorticoid replacement is necessary along with stabilization of the hemodynamic status with NaCl boluses and high dose parenteral glucocorticoids (100 mg hydrocortisone q 8h intravenous). Unless significant cerebral edema is present, hydrocortisone rather than dexamethasone is preferred. The recent UK guidelines recommend surgical decompression in case of "significant neuro-ophthalmic signs or reduced level of consciousness.".If conservative treatment is chosen, then careful monitoring of visual signs and symptoms is necessary, and surgical decompression is recommended if visual disorders do not improve or if they deteriorate.

Upto 80% of patients have residual hypopituitarism following apoplexy and will need hormone replacement. MRI of the pituitary should be obtained at 3-6 month intervals until the anatomy is stable and then yearly for 5 years. A month after discharge from the hospital and recovery from the acute event, patients are subject to repeat endocrine testing to determine need for long-term hormone replacement therapy.

5. Adrenal Insufficiency

Adrenal insufficiency (AI) is a disorder characterized by the failure of adrenocortical function resulting mainly in impaired secretion of glucocorticoids (GCs) only or of GCs and mineralocorticoids (MCs). It can be either primary or secondary (pituitary)

Acute adrenal insufficiency, also termed adrenal crisis, is one of the most severe endocrine emergencies. Primary adrenal insufficiency (PAI) (also termed Addison's disease), is due to the inability of the adrenal cortex to produce sufficient amounts of glucocorticoids and/or mineralocorticoids. Secondary adrenal insufficiency results from deficient adrenal glucocorticoid production only, because of ACTH deficiency due to impairment of hypothalamic-pituitary axis (i.e., hypopituitarism). The commonest cause is prolonged use of glucocorticoids due to various reasons that suppress the HPA axis.

Etiology

Commonest cause of PAI is autoimmune adrenalitis. It used to be tuberculosis. Other causes include fungal infections, infiltrative disorders, adrenal hemorrhage, retroviral therapy for HIV and genetic causes like CAH, adrenal hypoplasia congenital disorders like adrenoleukodystrophy or syndromes like Triple A syndrome.

Secondary adrenal insufficiency can occur as the result of hypopituitarism, hypothalamic dysfunction, space occupying lesions or most commonly, prolonged use of glucocorticoids.

Clinical Features

PAI often presents acutely with hyperpigmentation, hypotension, hyperkalemia, hypoglycemia, hyponatremia, fever, severe dehydration and often shock. Hyperpigmentation occurs in more than 90% of persons with PAI, and helps to differentiate PAI from secondary adrenal insufficiency.

Diagnosis

The initial laboratory evaluation of patients should include a determination of plasma glucose, blood urea nitrogen (BUN, or urea), creatinine, electrolytes, urinalysis, complete (full) blood count and ESR. An electrocardiogram (ECG), chest X-ray, urine and blood cultures should also be considered, especially in the setting of sepsis. Endocrine evaluation includes, thyroid profile, ACTH and 8 AM cortisol. Secondary adrenal insufficiency warrants evaluation of other pituitary hormones also. Synacthen test is used where indicated especially in secondary adrenal insufficiency.

Treatment

Acute adrenal crisis follows the principle of replacement of 5 S's

1. Salt replacement – Sodium is lost in urine due to mineralocorticoid deficiency and needs to be replaced with normal saline.
2. Sugar replacement –Glucose to prevent hypoglycemia
3. Steroid –Hydrocortisone is used to replace glucocorticoid deficiency

4. Supportive care – including fluid replacement and inotropes
5. Seek precipitants –usually infection or hemorrhage

Initial hydrocortisone dose is 100 mg hydrocortisone as an IV injection, followed by 100–200 mg hydrocortisone in glucose 5% per continuous IV infusion. In continued adrenal insufficiency, hydrocortisone 15-25 mg/day in divided doses needs to be given daily with addition of fludrocortisone 50-200mcg daily in PAI. Salt rich diet should be encouraged.

Follow-up

Patients with chronic AI should be followed-up closely by an endocrinologist with monitoring and mapping of glucocorticoid and mineralocorticoid doses and further etiological evaluation. Steroid bracelets and sick day instructions to double the dose of glucocorticoids during sickness should be provided. Patients should be educated to have a steroid card or bracelet with the name and phone number of a care provider and an emergency pack with hydrocortisone to treat an emergency.

6. Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS; or hyperosmolar non ketotic hyperglycaemia) are the most common and most serious endocrine emergencies. DKA is a triad of hyperglycaemia, ketosis and acidemia, and the diagnostic criteria, as defined by the American Diabetes Association, are blood glucose >13.8 mmol/l (250 mg/dl), pH <7.30, serum bicarbonate <18 mmol/l, anion gap >10, and ketonaemia. HHS is caused by inadequacy of insulin and defined as blood glucose >33.3 mmol/l (600 mg/dl), pH >7.30, bicarbonate >15 mmol/l, serum osmolality >320, and a small amount of ketones may be present. They are not restricted to Type 1 diabetes and can be present in any Type of diabetes. Worldwide the most common precipitating cause of DKA and HHS is infection, being responsible for nearly half the cases.

Pathology

The pathogenesis of DKA or HHS comprises insulin

deficiency with increased counter regulatory hormones of glucagon, catecholamines, cortisol and growth hormone leading to increased glucose production in the liver and decreased utilisation in peripheral tissues. In DKA, the severe deficiency in insulin and increased counter regulatory hormones lead to increased lipolysis and production of ketone bodies and resulting metabolic acidosis.

Clinical features

The presenting symptoms are often vomiting and abdominal pain, with history of polyuria, polydipsia and weight loss. The mechanisms of abdominal pain are poorly understood, but include delayed gastric emptying, ileus, oesophagitis with ulceration, subacute pancreatitis, hepatic capsule expansion or bowel ischaemia. Hypotension, altered sensorium, fever—especially in the setting of infection, fruity odour on breath and Kussmaul's breathing are typical. Confusion is much more common in HHS.

Diagnosis

Diagnostic criteria are as mentioned earlier and are laid down by ADA. DKA can impair lipoprotein lipase activity, resulting in gross elevation of triglyceride causing a pseudohyponatraemia. Although there is a potassium deficit at presentation, the measured serum potassium can be normal or raised due to a shift of potassium from intracellular to extracellular space after the shift in water. Mild leukocytosis is often seen, but a leucocyte count $>25\text{,}000\text{ mm}^3$ is suggestive of an underlying bacterial infection.

Treatment

The treatment goals for DKA and HHS are to correct the fluid depletion, decrease the blood glucose level, correct the electrolyte imbalance and treat the precipitating causes. Most DKA are mild to moderate and can be nursed in high dependency units, especially if detected early. Sicker patients can be managed in an ICU. It is necessary to establish a local protocol for DKA and HHS management.

Most protocols start with isotonic saline infusion to restore renal perfusion with 1000–1500 ml fluid

given within the first hour. This lowers the plasma osmolality and reduces the blood glucose levels.

Insulin promotes glucose utilisation in peripheral tissues and lowers hepatic glucose production, reducing blood glucose levels. Insulin also counters ketogenesis and inhibits the release of free fatty acids, thereby correcting the acidosis. The use of low dose intravenous insulin infusion (initially 6 unit/h) is now standard of care and allows for a sustained and easily reversible fall in blood glucose concentration. To prevent development of hypokalaemia after initiation of treatment for DKA, potassium replacement should be started after the first litre of fluid, aiming to maintain the concentration between 4 and 5 meq/l. Bicarbonate replacement in patients with DKA remains controversial and is not recommended unless if the pH is <7 .

Once ketosis has subsided and acidosis has normalized, transition from continuous insulin infusion to subcutaneous insulin injection needs to be done. It is quite tricky and often needs regular adjustments and multiple daily injection regimen and may require regular endocrine follow-up. The criteria for resolution of DKA as proposed by the American Diabetic Association are glucose level $<11\text{ mmol/l}$ (200 mg/dl), venous bicarbonate $>18\text{ mmol/l}$ and venous pH >7.30 . Also, insulin infusion should not be stopped until patients are able to eat and drink normally. Patients with known diabetes can then be restarted on the current subcutaneous insulin regimen. The subcutaneous insulin needs to be started at least 1 h before the discontinuation of insulin infusion to avoid rebound hyperglycaemia and even DKA.

If properly educated, upto 50% of DKA admissions may be prevented and hospital admissions reduced.

7. Hypoglycemia

Hypoglycemia is uncommon in people who are not being treated for diabetes mellitus. Symptomatic hypoglycemia is diagnosed clinically using Whipple's triad: symptoms of hypoglycemia, plasma glucose concentration $<55\text{ mg/dl}$ (3.0 mmol/l), and resolution of those symptoms after the plasma glucose concentration is raised.

Etiology

Hypoglycemia in diabetes is typically the result of treatments that raise insulin levels and thus lower plasma glucose concentrations (use of insulin, sulphonylureas or glinides.). In adults not taking glucose-lowering drugs to treat diabetes mellitus, critical illnesses, hormone deficiencies, islet and non-islet cell tumors and factitious hypoglycemia should be considered.

Clinical Features

Although there are no specific symptoms of hypoglycaemia, they can be grouped as either autonomic (ie, sweating, warmth sensation, anxiety, nausea, palpitation and even hunger) or related to neuroglycopenia (ie, tiredness, being uncoordinated, visual disturbances, drowsiness, altered behaviour, confusion, and, if left untreated, coma and seizures). The autonomic symptoms tend to occur first, and neuroglycopenia later.

Treatment

Immediate treatment should be focused on reversing the hypoglycemia. If the patient is able to ingest carbohydrates 15 grams of glucose should be given every 15 minutes until the hypoglycemia has resolved. If the patient is unable to ingest carbohydrates, or if the hypoglycemic episode is severe, then parenteral glucose should be administered, ideally 25 gram boluses of 50% dextrose followed by 10% dextrose maintenance. Glucagon injections can be given in children and in out patient or primary care setting, but should immediately be followed by a meal to prevent rebound hypoglycemia. Sublingual placement of carbohydrates (i.e., hard candy) in an unconscious patient should be avoided as this can increase the risk of aspiration.

Once a patient has had a severe episode of hypoglycaemia, he or she may have impaired recognition of hypoglycaemia symptoms over the subsequent 24 hours and so needs regular monitoring of blood glucose levels. The most important step in the management of hypoglycaemia is to identify the cause to prevent future episodes with education and support.

8. Other emergencies are also rarely encountered like hypertensive and pheochromocytoma associated emergencies, amiodarone induced thyrotoxicosis, hypercalcemia, kidney stone emergencies and Sight-Threatening Graves' Ophthalmopathy but for reasons of brevity the discussion is restricted to the above few endocrine emergencies and a list of additional reading resources are provided at the end of the chapter to address these other less common emergencies.

In conclusion, diabetic and endocrine emergencies are often treated by the acute care team or emergency department or the primary care physician. Most common disorders encountered are DKA and hypoglycemia. However, complacency should not be encouraged and is particularly important to follow guidelines and to involve the endocrine team in identification and management. Many endocrine emergencies are not common, but nonetheless important simply because of their rarity. A high level of suspicion is often required to make a diagnosis, and treatment must be started before the diagnosis can be confirmed. Team approach and appropriate referrals should be the norm rather than the exception. If identified early, endocrine emergencies are easily treated and every opportunity to save lives should be utilized.

Further reading

1. Kearney T, Dang C. Diabetic and endocrine emergencies. Postgrad Med J. 2007 Feb;83(976):79-86.
2. Cryer PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Sequist ER, Service FJ. Evaluation and Management of Adult Hypoglycemic Disorders: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 94:709-728, 2009.
3. Liamis G, Milionis HJ, Elisaf M. J Bone Miner Metab. 2009;27(6):635-42. A review of drug-induced hypocalcemia.
4. Chen YJ, Hou SK, How CK, et al. Diagnosis of unrecognized primary overt hypothyroidism in the ED. Am J Emerg Med 2010;28:866-870

5. Vanderpump M¹, Higgins C, Wass JA. UK guidelines for the management of pituitary apoplexy a rare but potentially fatal medical emergency. *Emerg Med J.* 2011 Jul;28(7):550-1
6. Glenn Matfin. Endocrine and metabolic medical emergencies : a clinician's guide Second edition., Hoboken, NJ : Wiley, 2018

TABLE 1 : Precipitating factors for Thyroid Storm

S.No.	Precipitating factor
1	Infections
2	Surgery –either thyroid or non-thyroid surgery
3	Sudden cessation of anti-thyroid medications
4	Recent use of iodinated contrast
5	Radioiodine therapy
6	Acute illnesses and Pregnancy particularly during labor and delivery

TABLE 2 : Etiology of hypocalcemia

S.No	Cause
1.	Hypoparathyroidism
2.	Magnesium deficiency
3	Chronic Kidney disease
4	Hyperphosphatemia
5	Vitamin D deficiency
6	Hungry Bone Syndrome
7	Sepsis
8	Drugs
9	Citrate or EDTA in context of transfusions
10	Pseudohypoparathyroidism secondary to G-protein defects
11	Malabsorption
12	Osteoblastic metastases
13	Pancreatitis
14	Calcium-sensing receptor (CaSR) constitutive activating mutations



Acute Severe Asthma

Dr Rajeeva Moger

Consultant Physician

Apollo Hospitals, Bangalore

rajeevamoger@gmail.com

Bronchial asthma is a worldwide problem. According to Global Burden of Disease (GBD, 1990–2019) India has an estimated 34.3 million asthmatics, accounting for 13.09% of the global burden. Asthma is responsible for 27.9% of disability – adjusted life years (DALYs) and 13.2 per thousand deaths in India. A lot of people in India still consider asthma a stigma and do not reveal the disease. Although Inhaled Corticosteroids (ICS) are the mainstay of asthma treatment, many patients refuse ICS thinking that they are strong medicines and habit forming which they will have to take lifelong. This is one of the important reasons for inadequate treatment, frequent exacerbations and also frequent visits to emergency department/hospitalization. Top three states in India with highest number of asthma patients are Uttar Pradesh, Bihar and Orissa (1).

The factors influencing asthma morbidity and mortality are socioeconomic status, ethnicity, urban dwelling, smoking and other comorbid medical conditions (2).

The common triggering factors of an acute episode of asthma are discontinuation of medications, severe psychological stress, exposure to dust, pollens, pets, polluted air, exercise, infections, changes in weather, and certain medications like aspirin, beta blockers and NSAIDs.

Pathology and Immunobiology

The typical gross anatomic features seen in those with asthma are airway narrowing, increased mucus secretion occluding the lumen and cellular infiltration of the airway walls, hyperinflation, and atelectasis. Microscopically, exudation of plasma proteins, oedema of mucosal and submucosal

region, bronchial smooth muscle hypertrophy and hyperplasia of the microvasculature, injury and desquamation of the epithelium, and thickening of the subepithelial collagen layer are seen. (3)

Clinical Features

Most patients with acute asthma present with a combination of symptoms consisting of cough, chest tightness, breathing difficulty and wheezing. However, there is no uniformity in symptoms. The physical signs that are commonly present are diaphoresis, cyanosis, use of accessory muscles, tachypnoea, tachycardia, wheeze, hyperinflation, and in severe cases, pulsus paradoxus and obtundation. Sweating, the use of accessory muscles, a paradoxical pulse, and the inability to communicate in full sentences are all associated with the presence of substantial airway narrowing. However, the absence of these signs does not rule out significant airway narrowing. Sometimes the patients with severe bronchospasm may have silent chest or minimal wheeze on auscultation. Patients with hypotension and severe tachycardia or bradycardia need urgent resuscitative measures and complications of acute severe asthma like pneumothorax should be excluded. The use of accessory muscles is observed in about 30% of cases at presentation, a paradoxical pulse in 15–20%, sweating in 12%, and cyanosis in less than 1%. Usually, clouding of consciousness is seen in severe hypoxemia and is an indicator of an impending catastrophe (4).

Severe asthma

According to consensus guidelines, an episode of asthma is considered to be severe if one or more of the following features are present:

evidence of accessory muscle activity, presence of a paradoxical pulse exceeding 25 mm Hg, tachycardia with a heart rate more than 110 beats/minute, tachypnoea with a respiratory rate more than 25–30 breaths/minute, inability to speak full sentences, a peak expiratory flow rate (PEFR) or $\text{FEV}_1 < 50\%$ of the predicted, and an arterial oxygen saturation less than 91–92% (5, 6).

Anyone of the following in a patient with severe asthma is indicative of life-threatening illness: Peak expiratory flow less than 33% of the predicted value, $\text{PO}_2 < 92\%$, $\text{PaO}_2 < 60 \text{ mm of Hg}$, normal PaCO_2 of 35 to 45 mm of Hg, silent chest, cyanosis, feeble respiratory effort, bradycardia, hypotension, exhaustion, confusion, coma (7).

Differential Diagnosis

Other conditions that can present with similar manifestations include chronic obstructive pulmonary disease, bronchiectasis, endobronchial obstructive lesions including foreign bodies, tracheal narrowing, pulmonary oedema, pneumonia, and pulmonary thromboembolism(8).

Evaluation

The critical component of managing acute episodes of asthma is a rapid and accurate assessment of the patient's condition and stabilization of the patient as early as possible by ensuring adequate oxygenation and reversal of bronchospasm with optimum medications. Assess the airflow limitation objectively, evaluate the severity and assess the adequacy of gas exchange.

Assess exacerbation severity while starting SABA and oxygen. Assess dyspnoea, respiratory rate, pulse rate, oxygen saturation and lung function. Consider alternative causes of acute breathlessness (e.g., heart failure, upper airway dysfunction, inhaled foreign body or pulmonary embolism). Immediately give inhaled SABA, inhaled ipratropium bromide, oxygen and systemic corticosteroids. Start treatment with repeated doses of SABA usually by nebulization, and controlled flow oxygen if available. Check response of symptoms and saturation frequently, titrate oxygen if needed to maintain target saturation of

93–95% in adults.

Arterial blood gas analysis is necessary in patients with hypoxia (SPO_2 less than 90%) at presentation, in those who develop hypoxia immediately after arrival in emergency room or in those who deteriorate after initial treatment. The most common blood gas abnormality seen in acute asthma is type I respiratory failure - combination of hypoxemia, hypocapnia, and respiratory alkalosis. Modest elevation of CO_2 , averaging from 10 to 15 mmHg above normal, is observed in about 10% of patients. This is generally associated with severe reduction in FEV_1 (20% or less of predicted FEV_1). Normocarbia is seen in about 15 to 20% of cases and should be considered as impending respiratory failure (9).

Treatment of asthma exacerbations

Oxygen

Correction of hypoxemia is very important in acute exacerbations of asthma, although severe hypoxemia is rare. We should aim for SPO_2 of more than 92% and correction should be started immediately with 2 to 4 L/minute of oxygen supplementation by nasal cannula or oxygen mask. Monitor the SPO_2 frequently and titrate the oxygen supplementation accordingly.

Beta 2 Agonists

High dose inhaled β_2 agonist are first line agents and should be delivered as early as possible in an acute asthma attack. Oxygen driven nebulizers are the preferred method compared to air driven compressor nebulization. Inhaled β_2 agonists are as effective as intravenous β_2 agonists in adults with acute asthma. Short acting β_2 agonists (SABA) like salbutamol, levosalbutamol and terbutaline provide quick relief of bronchoconstriction and asthma symptoms. They have rapid onset of action and provide three to four times more bronchodilatation compared to anticholinergics and methylxanthines, hence, they are the first-line treatment for acute illness. They can be given as continuous nebulization if the response to initial bolus nebulization is suboptimal (10). Tremors of the hands and tachycardia are the commonly noticed adverse drug events.

Anticholinergics.

The release of acetylcholine stimulates muscarinic receptors to produce bronchoconstriction and mucous secretion (11). Ipratropium bromide has a slow onset of action (60–90 minutes to peak) and medium potency (about 15% increase in PEFR). Apart from dryness of mouth and bitter taste, it does not induce systemic side effects. When combined with a nebulised α_2 agonist, it has been shown to produce significantly greater bronchodilatation than a α_2 agonist alone, hence, used as add on therapy or second-line therapy (12).

Steroid Treatment

Inhaled corticosteroids (ICS) are mainstays in prevention of exacerbations. The use of ICS in chronic asthma reduces symptoms, improves lung function, decreases exacerbations and also reduces the need for hospitalizations. Patients who respond inadequately to inhaled beta agonists require urgent treatment with systemic corticosteroids (parenteral or oral). The dose and duration of steroid therapy varies with the clinical situation. The usual daily doses of corticosteroids are 30 to 60 mg prednisolone, 200 to 400 mg of hydrocortisone or 40 to 120 mg of methylprednisolone and can be withdrawn abruptly if the total duration of treatment is less than 14 days (13, 14).

Magnesium sulphate

Magnesium is an important cofactor in many enzymatic reactions and hypo and hypermagnesemia can cause contraction and relaxation of smooth muscles, respectively. Intravenous infusion of 1 to 2 g of magnesium sulphate over 30 to 45 minutes can be used in patients who have not had good response to treatment with bronchodilators and steroids. However, there is insufficient evidence to support the routine use of magnesium sulphate in acute exacerbations of asthma (15).

The methylxanthines

Aminophylline and theophylline were commonly used in the treatment of acute asthma in the past. They are significantly less effective than beta agonists and anticholinergics. Although they have anti-inflammatory actions, they have significant side effects such as palpitation, arrhythmia and vomiting and they should be avoided in high-risk

cardiac patients (16).

Antileukotriene agents

Antileukotriene drugs like zafirlukast and montelukast have limited but favourable data for the use of these agents in acute asthma. IV Montelukast reduced treatment failures, reduced steroid use in the emergency department and finally reduced α_2 agonist doses. (17, 18)

Mechanical ventilation

Non-invasive ventilation or invasive ventilation should be considered in patients with persistent hypoxemia, carbon dioxide retention or altered sensorium. The goal for ventilation in asthma is to relieve hypoxemia and to minimise hyperinflation. A number of prospective randomized trials have shown that non-invasive ventilation (NIV) reduces the need for endotracheal intubation, length of hospital stay and in-hospital mortality rate, and even that it improves long-term survival. It is currently being used as an initial alternative to mechanical ventilation in some centres.

Non-invasive Positive Pressure Ventilation (NPPV) may offer short-term support for some subjects with hypercapnic respiratory failure who can cooperate with their care and are able to protect their airways (19).

The commonly accepted contraindications to NPPV are as follows: cardiac or respiratory arrest, severe encephalopathy, haemodynamic instability, facial surgery/deformity, high risk for aspiration, non-respiratory organ failure, severe upper gastrointestinal bleeding, unstable arrhythmia, and upper airway obstruction. The decision to intubate should be based mainly on clinical judgement. Markers of deterioration include rising carbon dioxide levels (including normalization in a previously hypocapnic patient), exhaustion, mental status depression, haemodynamic instability and refractory hypoxaemia (20).

Post discharge follow up after an exacerbation

Exacerbations often represent failure in chronic asthma care, and they provide opportunities to review the patient's asthma management. All patients must be followed up regularly by a health care provider until symptoms and lung function

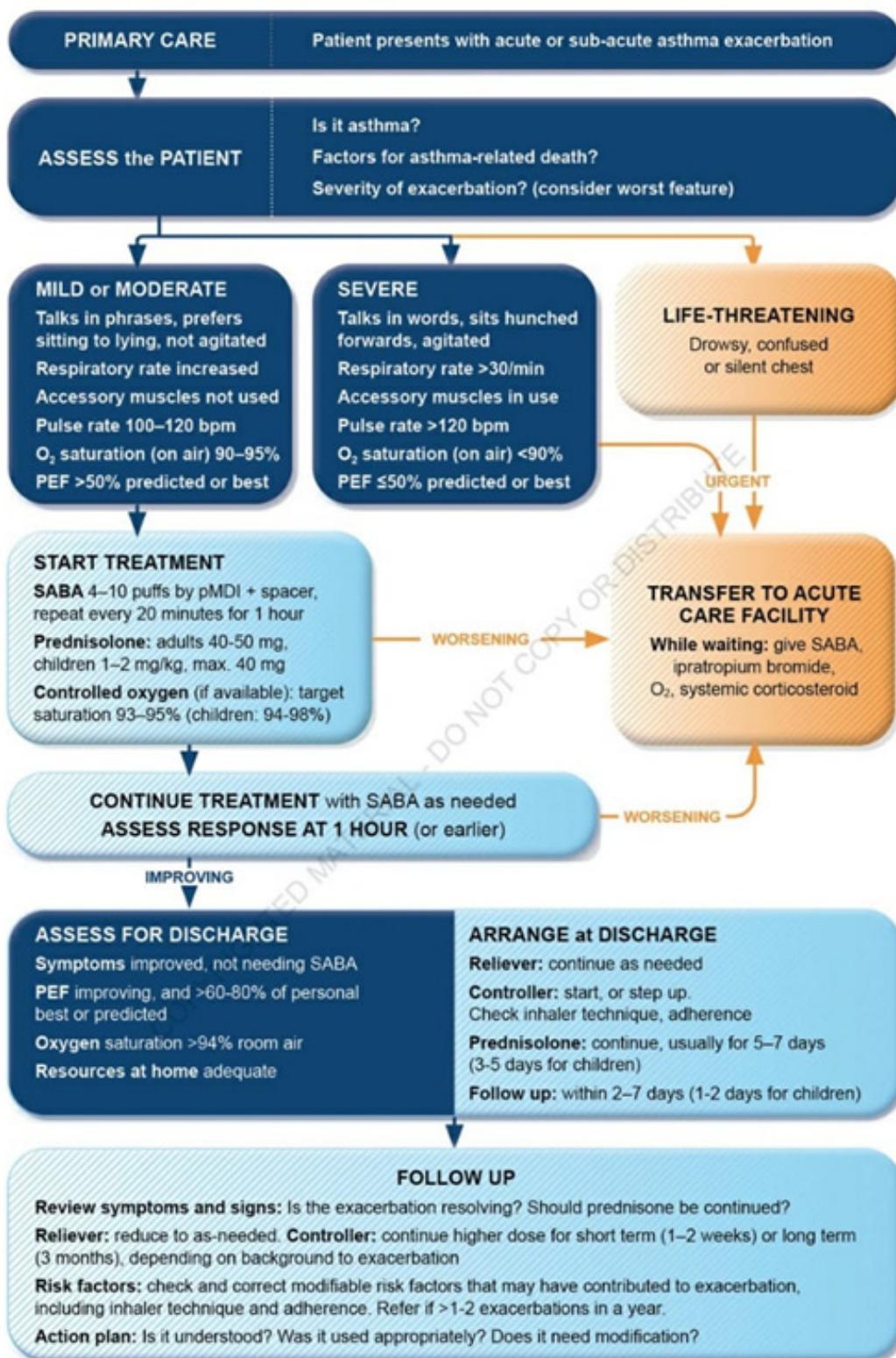
return to normal. Take the opportunity to review:

- The patient's understanding of the cause of the exacerbation
- Modifiable risk factors for exacerbations, e.g. smoking
- Understanding the purpose of medications, and inhaler technique skills
- Adherence with ICS and OCS as this may fall rapidly after discharge.
- Written asthma action plan – revise if necessary (21).

References

1. GBD Compare. Viz Hub . (2021, June 30). <https://vizhub.healthdata.org/gbd-compare/>
2. Weiss KB, Wagener DK. Changing patterns of asthma mortality. *JAMA* 1990;264:1683–1687.
3. Messer J, Peters GA, Bennet WA. Cause of death and pathological findings in 304 cases of bronchial asthma. *Dis Chest* 1960;38:616-624.
4. National asthma council. Asthma management handbook, 5th ed. Melbourne, Australia: National asthma council Australia; 2002
5. National Asthma Education and Prevention Program Expert Panel. National Asthma Education and Prevention Program Expert Panel Report II: guidelines for the diagnosis and management of asthma. NIH Publication 97-4051. Bethesda, MD: National Institutes of Health; 1997.
6. British Thoracic Society. Guidelines on the management of asthma. *Thorax* 1993;48:S1–S24.
7. Raja Dhar, AG Ghoshal. Management of Acute Severe Asthma march 2014, volume 62 special issue.
8. Miller TP, Greenberger PA, Patterson R. The diagnosis of potentially fatal asthma in hospitalized adults: patient characteristics and increased severity of asthma. *Chest* 1992; 102:515-518.
9. McFadden ER Jr, Lyons HA. Arterial-blood gas tension in asthma. *N Engl J Med* 1968;278:1027-1032.
10. Laube BL, Janssens HM, de Jongh FH, et al. What the pulmonary specialist should know about the new inhalation therapies. *Eur Respir J* 2011;37:1308 1331.
11. Fryer AD. Muscarinic receptors. In: Busse WW, Holgate ST, editors. *Asthma and rhinitis*, 2nd ed. London: Blackwell Science; 2000. p. 914–926.
12. Gross NJ, Skorodin MS. Anticholinergic, antimuscarinic bronchodilators. *Am Rev Respir Dis* 1984;129:856–870.
13. Rowe BH, Edmonds ML, Spooner CH, et al. Corticosteroid therapy for acute asthma. *Respir Med* 2004;98:275 284.
14. Rowe BH, Spooner C, Ducharme FM, et al. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev* 2001;1:CD002178.
15. Cochrane library 28 may 2014.
16. Ron M. Walls MD, in Rosen's Emergency Medicine: Concepts and Clinical Practice, 2018.
17. Siverman RA, Chen Y, Bonuccelli CM, Simonson SG. Zafirlukast improves emergency department outcomes after an acute asthma episode [abstract]. *Ann Emerg Med* 1999;34:S1.
18. Camargo CA Jr, Smithline HA, Malice MP, Green SA, Reiss TF. A randomized controlled trial of intravenous montelukast in acute asthma. *Am J Respir Crit Care Med* 2003;167:528–533.
19. Meduri GU, Cook TR, Turner RE, Cohen M, Leeper KV. Noninvasive positive pressure ventilation in status asthmaticus. *Chest* 1996;110:767–774.
20. Mountain RD, Sahn S. Clinical features and outcomes in patients with acute asthma presenting with hypercapnia. *Am Rev Respir Dis*. 1988;138:535–539.
21. GINA pocket guidelines 2020.

Management of Asthma exacerbations in primary care



O₂: oxygen; PEF: peak expiratory flow; SABA: short-acting beta₂-agonist (doses are for salbutamol)

Copied from GINA pocket guidelines2020



APPROACH TO ACUTE FLACCID PARALYSIS

Dr Praveen Kumar Yadav

Senior Consultant Neurologist

Director Aarogyam Neuroclinic,Durgapur,

Associate Professor in Medicine, SRIMS, Durgapur

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Acute flaccid paralysis (AFP) is a clinical syndrome characterized by rapid onset of weakness of lower motor neuron type, including weakness of the respiratory and pharyngeal muscles, progressing to maximum severity within several days to weeks. AFP is a complex clinical syndrome with a broad array of potential etiologies that vary remarkably with age. It may involve at least one or two or all limbs.

Accurate diagnosis of the cause of AFP is important for therapy and prognosis. If untreated, AFP may not only persist but also lead to death due to failure of respiratory muscles. It can also cause many complications like aspiration pneumonia, deep venous thrombosis, bed sores and contractures. It is also of great public health importance because of its use in surveillance for poliomyelitis in the context of the polio eradication initiative.

Guillain-Barry syndrome (GBS) is the most important clinical cause of AFP [1,2]. Studies from all around the world has found prevalence of GBS among acute flaccid paralysis patients of 42-47%[3] Studies around the world have identified envenomation, prophyria, hypokalemia, early acute transverse myelitis, rhabdomyolysis, botulism, and myasthenia gravis as other causes of acute flaccid paralysis. Neuroparalytic snakebite has been previously reported as a significant cause of acute flaccid paralysis in young rural men from Northern India.[4]

Males are at a higher risk for snake envenomation due to occupational and recreational outdoor activities that predispose them to encounters with venomous snakes. The reasons for such a predilection are not clear. Male preponderance in

GBS cases has been reported in various studies and our study reflects similar result [5,6].

A preponderance of younger individuals was observed among the cases of acute flaccid paralysis .60.8% were less than 40years of age with 28.9% between the age group of 40-60.

During monsoon a peak incidence upto 35% was seen while rest of the year the proportion of cases were similar throughout the year. Similar observation was seen in study by Kaur et al [7]. Sharma et al. who reported a peak incidence between June–July and Sept–October [8] and Sriganesh K et al. in 2013, who reported increased occurrence of GBS during the months of June to August [9].

Hence, in patients presenting with ascending paralysis, a diagnosis of GBS should be considered and in those with external ophthalmoplegia/ bilateral LMN facial palsy at presentation along with flaccid paralysis, diagnosis of GBS is more likely. GBS and snake envenomation accounted for 100 % of patients with bulbar paralysis. Bulbar weakness was seen in 26.66% of neuroparalytic snakebite patients, which is lower than that reported in previous retrospective studies [10]. Cranial nerve involvement was seen in 24.4% cases of GBS with cranial nerve VII involved in most of the cases as against 50% in a study by Morris et al [11] to 21% in a study by Olive et al. [12] with CN VII most often affected.

Patients with axonal variants of GBS who have more severe illness may also have contributed to the higher mechanical ventilation [13].

Hypokalemic periodic paralysis is a very important cause of acute flaccid paralysis and 48 % has a

secondary cause requiring detailed evaluation[14]

Hypokalemic paralysis in Sjogren's syndrome may precede the more classic clinical findings and serves as a clinical marker for this diagnosis [15]

Thyotoxicosis related periodic paralysis is also an important secondary cause for the same.

Table-1 –Causes of Acute Flaccid Paralysis

Infectious
Poliomyelitis
Vaccine-associated paralytic polio
Vaccine-derived poliomyelitis
Nonpolio enteroviruses
West Nile virus
Diphtheria
Myelopathic
Postinfectious transverse myelitis
Anti-MOG associated myelitis
Anti-AQP4 associated myelitis
Arterial or venous spinal cord infarction
Compression from spinal abscess, hemorrhage, or tumor
Neuropathic
Guillain-Barré syndrome
Acquired motor axonal neuropathy
Acquired motor sensory axonal neuropathy
Mononeuritis multiplex
Multifocal motor neuropathy
Acute intermittent porphyria
Toxic neuropathies
Disorders of neuromuscular transmission
Myasthenia gravis
Lambert-Eaton myasthenic syndrome
Botulism
Tick paralysis
Myopathic
Inflammatory myopathy
Rhabdomyolysis
Carnitine deficiency
Periodic paralysis

CLINICAL CLUES

History: Following points in the history must be enquired into so as to classify the presenting pattern of weakness (as given below). This helps not only finding the underlying etiology but also the prognosis and deciding the therapy:

- Onset & progression of weakness: sudden, acute (over hours), subacute (days to weeks)
- duration of weakness (hours to days to weeks) • pattern of weakness (eg: proximal, distal)
- pattern of progression (eg: onset in arms, "ascending paralysis")
- sensory involvement (numbness, tingling, loss of balance esp. in dark, pain / burning bulbar involvement (change in voice or swallowing)
- facial weakness (trouble chewing, sucking with straw, blowing)
- extraocular muscle weakness (diplopia) or ptosis
- respiratory involvement (ability to complete sentences, dyspnea, orthopnea)
- bladder or bowel involvement
- autonomic involvement (diarrhea, orthostatic dizziness, urinary retention, palpitations)
- systemic symptoms (fever, weight loss, rash, joint pain)
- recent illness or immunization (diarrheal or respiratory tract infection, anti rabies vaccine, oral polio vaccine)
- recent travel (out of country, to woods [tick bites])
- recent h/o dog bite
- precipitating factors (exertion, carbohydrate loading - with periodic paralyses) • fluctuation in weakness (eg. diurnal variation, fatigability in myasthenia)
- drug or toxin exposure (canned or 'bad' food, pesticides, lead exposure)

- family history (porphyria)

PHYSICAL EXAMINATION

- Distribution and degree of weakness looking specially for extraocular muscles, facial muscles and bulbar involvement
- Assess for fatigability
- Sensory impairment: particular modality (vibration / proprioception vs. pain / temperature) - is there a sensory level?
- Reflexes: Are the deep tendon reflexes lost? (ie. areflexic), depressed, preserved, or brisk; Do diminished reflexes facilitate with repeated efforts? (LEMS)
- Autonomic features (postural fall, abnormal sweating, pupillary response, ileus)
- Skin: lines on nails with arsenic poisoning (Mee's lines), ticks, photosensitivity, Gottron's papules on extensor surfaces & heliotrope discoloration over eyelids (dermatomyositis), fang marks
- Spinal tenderness (with epidural abscess or hematoma, spinal tumour)
- Straight leg raise (radiculopathy)

CLINICAL CLUES TO DIFFERENTIAL DIAGNOSIS

Step 1: Is it an upper motor neuron (UMN) or a lower motor neuron (LMN) lesion Clues to UMN lesion (mostly a spinal cord lesion) could be presence of either:

- Brisk reflexes
- Extensor plantar
- Definite sensory level
- Bladder or bowel involvement

A LMN lesion will have absent reflexes with mute plantar. Frequently, an acute onset spinal cord lesion may present with absent reflexes due to spinal shock. But the presence of other differentiating features (extensor plantar, definite sensory level and bladder involvement) help localize the lesion to spinal cord.

Step 2:

If it is a LMN lesion what is the pattern of weakness? Is it proximal or distal? Lesions localized to the following anatomical locations cause proximal, mostly symmetrical weakness in AFP:

- Muscle
- NMJ
- Polyradiculoneuropathies

Poly neuropathy will present with distal, mostly symmetrical weakness. Lesions localized to the anterior horn cells can present with symmetrical or asymmetrical, proximal, distal or a combination of both. The reflexes will be absent in both the conditions.

Step 3:

Are the reflexes preserved?

Localization of lesions with proximal weakness and preserved reflexes include muscle or NMJ.

Fatigability (appearance of weakness with repeated use) is a prominent feature in NMJ disorders especially myasthenia.

Reflexes would be absent in:

- Anterior horn cell disorders
- Polyradiculoneuropathies
- Neuropathies

Step 4:

Are sensations preserved?

Neuropathies present with sensory involvement.

Polyneuropathy presents with glove and stocking sensory involvement while mononeuritis multiplex would present with patchy sensory loss. Polyradiculoneuropathies may or may not have a sensory loss. Some GBS variants may have sensory loss. Cauda equina may present with a sensory loss in a radicular distribution

CATEGORIZATION AS PER PATTERN OF INVOLVEMENT

It is useful to classifying the pattern of involvement into any one of the following given below. This approach narrows the differential diagnosis further

1. Flaccid symmetric quadripareis (\pm bulbar and respiratory involvement) with areflexia and minimal to profound sensory loss (but often sensory symptoms) - Acute neuropathy or polyradiculopathy (eg GBS)
2. Symmetric proximal muscle weakness without sensory symptoms or signs and with preserved reflexes: Acute myopathy (eg. polymyositis); periodic paralysis
3. Fatigable muscle weakness with diplopia, ptosis and bulbar dysfunction (eg myasthenia and other neuromuscular disorders)
4. Flaccid Paraparesis with sensory level (often with reduced lower limb reflexes & bladder

dysfunction) - Cauda equina syndrome (painful), thoracic spinal cord lesions (eg. transverse myelitis, spinal cord infarct)

5. Bulbar predominant involvement: • Botulism • Myasthenia gravis • GBS • Snake bite
6. Ophthalmoplegia with motor weakness: • Miller-Fischer variant of GBS (areflexia) • Botulism & Tick paralysis • Snake Bite
7. Prominent autonomic dysfunction: • GBS • Paraneoplastic syndromes • Organophosphate toxicity (muscarinic cholinergic overstimulation) • Botulism

(Fig 1 & 3)

Conclusion

Acute flaccid paralysis is a diagnostic challenge as the causes may be various with different treatment modalities and prognosis. Hence a systematic approach in examination and evaluation is of utmost importance.

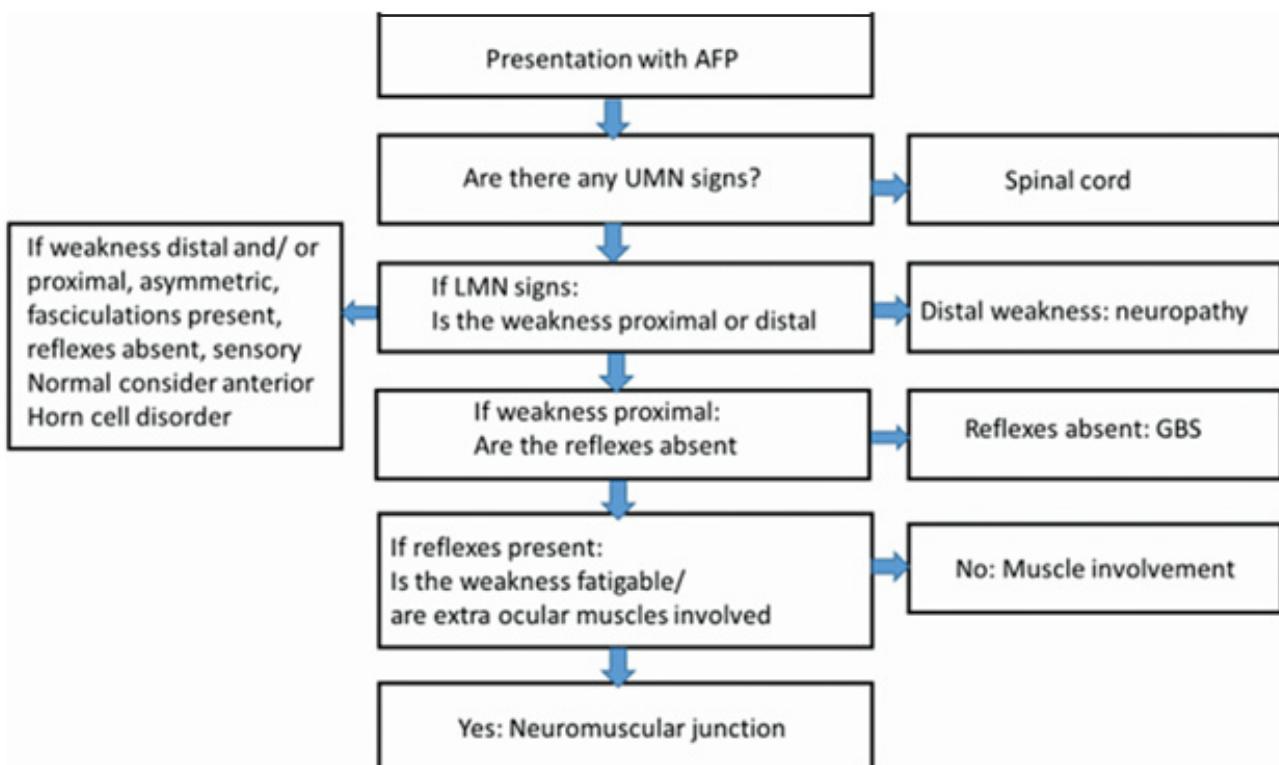


Fig 1-Approach to Acute Flaccid Paralysis

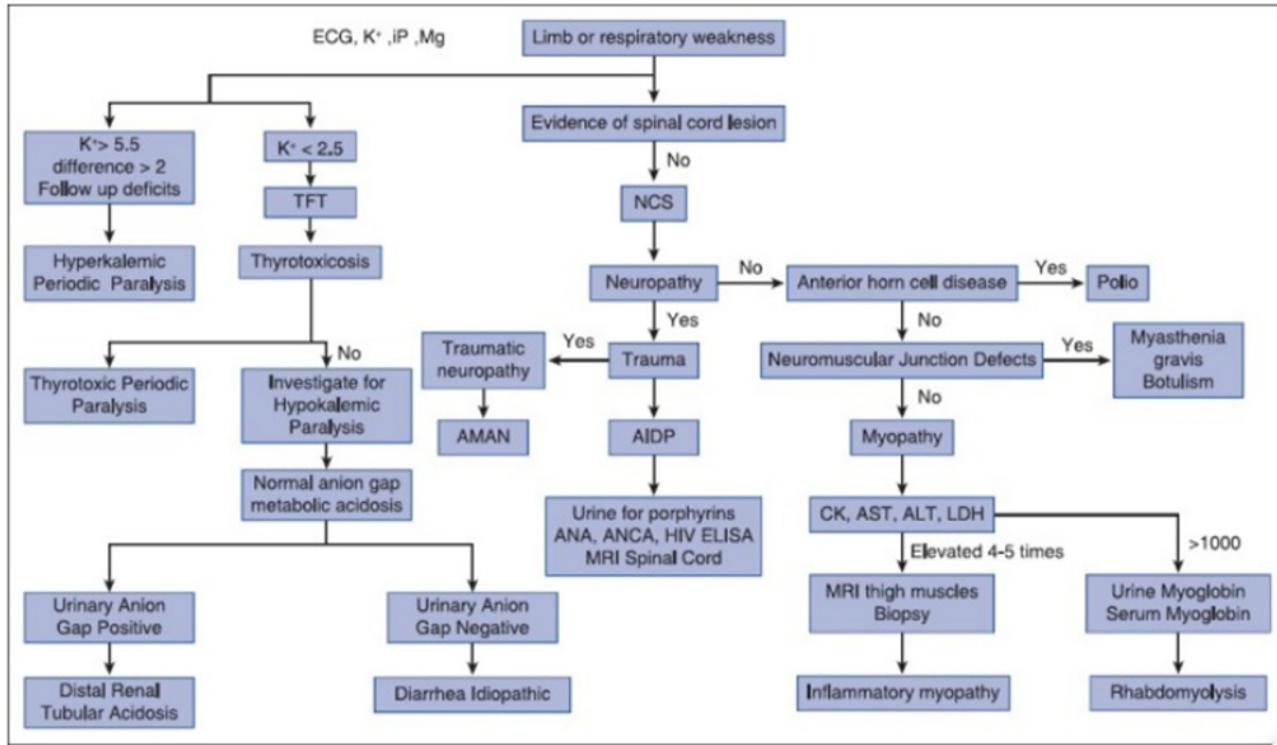


Fig 3-Sytematic Approach and evaluation of Acute Flaccid Paralysis

References

1. Morris AM, Elliott EJ, D'Souza RM, Antony J, Kennett M, Longbottom H. Acute flaccid paralysis in Australian children. *J Paediatr Child Health*. 2003;39:22-6.
2. Lam RM, Tsang TH, Chan KY, Lau YL, Lim WL, Lam TH, et al. Surveillance of acute flaccid paralysis in Hong Kong: 1997 to 2002. *Hong Kong Med J*. 2005;11:164-73.
3. Koul R, Chako A, Javed H, Al-Hinai K, Zachariah M, Bulusu S, et al. A profile of childhood neuropathies at a university hospital in Oman. *Saudi Med J*. 2002;23:450-6.
4. Sharma N, Chauhan S, Faruqi S, Bhat P, Varma S. Snake envenomation in a north Indian hospital. *Emerg Med J*. 2005;22:118-20. [PMCID: PMC1726667] [PubMed: 15662063]
5. Soysal A, Aysal F, Caliskan B, Dogan Ak P, Mutluay B, Sakalli N, et al. Clinico-electrophysiological findings and prognosis of Guillain-Barré syndrome—10 years' experience. *Acta Neurol Scand*. 2011;123:181-6
6. Arami MA, Yazdchi M, Khandaghi R. Epidemiology and characteristics of Guillain-Barré syndrome in the northwest of Iran. *Ann Saudi Med*. 2006;26:22-7.
7. Kaur U, Chopra JS, Prabhakar S, Radhakrishnan K, Rana S. Guillain- Barré syndrome. A clinical electrophysiological and biochemical study. *Acta Neurol Scand*. 1986;73(4):394-402.
8. Sharma A, Lal V, Modi M, Vaishnavi C, Prabhakar S. *Campylobacter jejuni* infection in Guillain-Barré syndrome: a prospective case control study in a tertiary care hospital. *Neurol India*. 2011;59(5):717-721.
9. Sriganesh K, Netto A, Kulkarni GB, Taly AB, Umamaheswara Rao GS. Seasonal variation in the clinical recovery of patients with Guillain Barré syndrome requiring mechanical ventilation. *Neurol India*. 2013;61(4):349-354.

10. Halawa EF, Ahmed D, Nada MA. Guillain-Barré syndrome as a prominent cause of childhood acute flaccid paralysis in post polio eradication era in Egypt. *Eur J Paediatr Neurol.* 2011;15:241–6. [PubMed: 21169042]
11. Durand MC, Porcher R, Orlikowski D, Aboab J, Devaux C, Clair B, et al. Clinical and electrophysiological predictors of respiratory failure in Guillain-Barré syndrome: A prospective study. *Lancet Neurol.* 2006;5:1021–8. [PubMed: 17110282]
12. Olivé JM, Castillo C, Castro RG, de Quadros CA. Epidemiologic study of Guillain-Barré syndrome in children
13. Govoni V, Granieri E. Epidemiology of the Guillain-Barré syndrome. *Curr Opin Neurol.* 2001;14:605-13.
14. Garg RK, Malhotra HS, Verma R, Sharma P, Singh MK. Etiological Spectrum of Hypokalemic paralisis: A retrospective analysis of 29 patients. *Ann Indian Acad Neurol.* 2013;16:365-70
15. Pous JM, Peyronnet P, Meur YL, Favereau JP, Charmes JP, Leroux- Robert C. Hypokalemic quadriplegia and respiratory arrest revealing primary Sjogren's syndrome. *Clin Nephrol.* 1992;37:189-91.



Concept of Treatment in Acute Stroke

Dr. Salil Uppal, Dr. Shikhil Uppal and Dr. Ashok Uppal

Uppal Neuro Hospital Multispecialty Centre and Research Institute,
Amritsar, Punjab
uppalashok14@gmail.com

An estimated one in four Indians is at risk of dying from a non-communicable disease (NCD) before reaching the age of 70. Stroke is one of the NCDs with high disease burden, representing a major cause of disability and death in the country. Stroke affects approximately 20 million people each year, resulting in 5 million fatalities.^{1,2} As per a Lancet study, stroke-related deaths in India in 2019, accounted for 7.4% of the total deaths in the country.³

The risk of disability or even death is increased when symptoms and treatment are not detected or treated timely, especially in cases of acute ischemic stroke. It is a medical emergency and patient should get treatment as soon as possible. BE FAST algorithm helps identify persons having an acute stroke who may present with following symptoms^{4,5}:

- B: Loss of Balance
- E: Loss of vision in one or both Eyes
- F: One side of the Face is drooping
- A: Feeling of weakness or numbness in one of the Arms
- S: Slurring of Speech
- T: Time to call the emergency services and get emergency care at the earliest

Prompt treatment can help to prevent further damage to brain and improve the chances of patient recovery. Human brain cells are rapidly lost as stroke progresses and that therapeutic interventions should be emergently pursued. In each minute, 1.9 million neurons are destroyed.^{6,7} This highlights the importance to act FAST. Additionally, it is also important to note the time when any symptoms first appear. This information

helps health care providers determine the best treatment.

How to treat stroke?⁹

On the way to the hospital

The key to stroke treatment and recovery is getting to the hospital quickly. Do not drive to the hospital. Let someone else drive you. Call an ambulance so that the medical staff can begin life-saving treatment on the way to the hospital.

At the hospital

At the hospital, health professionals will ask about the medical history and the time of symptoms onset. Brain scans will be done to know the type of stroke.

Treating ischemic stroke

For treating an acute ischaemic stroke patient, clot busting agent is injected which dissolves the clot and helps to resume the blood supply to the brain. However, the benefit of this treatment depends on the time interval between onset of symptoms and initiation of the treatment. More benefits are seen with early treatment with clot busting therapy. Hence, efforts should be taken by relatives to bring the patient to the hospital within 4.5 hours of symptom onset for better outcomes. Unfortunately, many stroke victims don't get to the hospital in time for treatment. Doctors may also treat ischemic stroke with other medicines, such as blood thinners, as well as surgery to remove the clot.

What to expect after a stroke?⁹

Although great progress can be made in regaining

independence after stroke, some problems may continue like:

- Paralysis (inability to move some parts of the body), weakness, or both on one side of the body
- Trouble with thinking, awareness, and attention
- Problems understanding or forming speech
- Trouble controlling or expressing emotions
- Numbness
- Pain in the hands and feet that worsens with movement and temperature changes
- Trouble with chewing and swallowing
- Problems with bladder and bowel control
- Depression

Recovering from stroke: stroke rehabilitation⁹

Rehabilitation helps ease the transition from hospital to home after a stroke. It begins in the hospital, often within a day or 2 after the stroke.

Recovery time after a stroke is different for everyone. Some people recover fully, but others have long-term or lifelong disabilities.

What is stroke rehabilitation?

Rehab can include working with speech, physical, and occupational therapists.

- Speech therapy helps people who have problems producing or understanding speech
- Physical therapy uses exercises to help you relearn movement and coordination skills that may be lost due to stroke
- Occupational therapy focuses on improving daily activities, such as eating, drinking, dressing, bathing, reading, and writing

Therapy and medicine may help with depression or other mental health conditions following a stroke. Support from family and friends can also

help alleviate fear and anxiety following a stroke.

How to prevent stroke?

If you have had a stroke, you are at high risk for another stroke. 1 in 4 stroke survivors has another stroke within 5 years.

That's why it's important to treat the underlying causes of stroke, including heart disease, high blood pressure, atrial fibrillation (fast, irregular heartbeat), high cholesterol, and diabetes. Choosing healthy diet, keeping healthy weight, regular physical exercise, limiting alcohol intake, smoking cessation, controlling diabetes, cholesterol, and blood pressure are some of the preventive measures for stroke.^{8,9}

References

1. THE STATE OF STROKE: A SURVEY ON AWARENESS ABOUT STROKE IN URBAN INDIA
2. Available from Preventing Stroke Deaths | VitalSigns | CDC as accessed on 26.10.2022
3. Available from Lancet study: Stroke caused nearly 7 lakh deaths in India in 2019, 7.4% of total deaths | Pune News (indianexpress.com) as accessed on 18.10.2022
4. About stroke. Available from About Stroke | cdc.gov as accessed on 17.10.2022
5. Stroke signs and symptoms. Available from Stroke Signs and Symptoms | cdc.gov as accessed on 17.10.2022
6. Stroke. 2017;48:479–481
7. Stroke. 2006; 37:263–266.
8. Available from Prevent Stroke: What You Can Do | cdc.gov as accessed on 17.10.2022
9. Available from Treat and Recover from Stroke | cdc.gov as accessed on 28.10.2022



Hypoglycemia

Dr. Jayanta Kumar Panda

Professor, PG Department of Medicine

Dr. Pradosh Kumar Sahu

SR, PG Department of Medicine

SCB Medical College, Cuttack, Odisha

Introduction

Hypoglycemia is the commonest diabetic emergency and is associated with considerable morbidity and mortality. The American Diabetes Association defines the hypoglycemia as any abnormally low plasma glucose concentration that exposes the subject to potential harm [1]. Hypoglycemia is common in insulin dependent diabetic patients and may also occur in patients with non-insulin dependent diabetes mellitus. It can be caused by too much insulin intake or oral hypoglycemic agents or too little food or excessive physical activity [2]. The National Electronic Injury Surveillance System study in older adults [3] found that nearly 25% of all medication-induced hospitalizations were due to insulin and oral hypoglycemic agents. These hospitalizations were largely preventable.

Minimizing hypoglycemia in diabetes is an important objective of the International Hypoglycemia Study Group (IHSG) and this can be achieved by acknowledging the problem, evaluating the risk factors, and applying the principles of intensive glycemic management.[4]

Definitions

Hypoglycemic events include all episodes of a plasma glucose concentration low enough to cause symptoms and/or signs, including impaired brain functioning and expose the individual to potential harm. However, the glycemic thresholds for hypoglycemia symptoms shift to lower plasma glucose concentrations in individuals with well controlled diabetes[5] and to higher plasma glucose concentrations in those with poorly controlled diabetes.[5,6] Hence, it is difficult to

assign a numerical value to hypoglycemia. The definitions as below are intended to guide clinical care and reporting and are based on glucose values detected by self-monitoring of blood glucose, CGM (for at least 20 minutes), or a laboratory measurement of plasma glucose.[7]

1. **Clinical hypoglycemia alert:** A glucose value of $\leq 3.9 \text{ mmol/L}$ (70 mg/dL) is an alert value that requires attention to prevent hypoglycemia. The alert can be used as the threshold value for identifying and treating hypoglycemia in children with diabetes because of the potential for glucose levels to drop further.
2. **Clinically important or serious hypoglycemia:** A glucose value of level $< 3 \text{ mmol/L}$ (58 mg/dL) indicates serious and clinically important hypoglycemia.[8,9] Those low levels may lead to defective hormonal counter regulation with subsequent increased risk of severe hypoglycemia. This level should be recorded in routine clinical care and reported in audit and in clinical trials of interventions directed toward reducing hypoglycemia as recommended by the IHSG. [4]
3. **Severe hypoglycemia** is defined as an event associated with severe cognitive impairment (including coma and convulsions) requiring external assistance by another person to actively administer carbohydrates, glucagon, or take other corrective actions. This aligns with the definition of severe hypoglycemia in adults in accordance with the American Diabetes Association Guidelines.[10]

This will also enable complete recording of events vs underestimation of severe hypoglycemia frequency in children if defined by coma or convulsions only. This expanded definition has also been used in children in previous observational studies on severe hypoglycemia.[11,12,13] However, as young children require assistance to correct even mild hypoglycemia, the event requires an assessment by the caregiver and clinician as to the presence or not of hypoglycemia-induced cognitive dysfunction. A subgroup of severe hypoglycemia is severe hypoglycemic coma, which is described as a severe hypoglycemic event resulting in coma or convulsion requiring parenteral therapy. These events should be recorded independently as these events are unequivocal and significant in outcome.

INCIDENCE OF HYPOGLYCEMIA

The exact incidence of hypoglycemia is difficult to ascertain, but mild hypoglycemia is common. Asymptomatic events are more likely to be unrecognized and underreported, while symptomatic hypoglycemia occurs on an average of 2 episodes per week with multiple such episodes in the lifetime. In contrast, the recall of severe hypoglycemia is more likely to be robust although variations in definitions, sample sizes, and retrospective surveys have made comparisons between studies difficult.

Hypoglycemia commonly occurs in clinical practice as approximately 90% of all patients who receive insulin have experienced hypoglycemic episodes [15]. Furthermore, surveys investigating the prevalence of hypoglycemia have provided some alarming results. The Diabetes Control and Complication Trial (DCCT) reported a threefold increase in severe hypoglycemia and coma in intensively treated T1DM patients versus conventionally treated patients [16]. A meta-analysis study reported that the prevalence of hypoglycemia was 45% for mild/moderate and 6% for severe. Incidence of hypoglycemic episodes per person-year for mild/moderate and for severe was 19 and 0.80, respectively. Hypoglycemia was prevalent among patients on insulin; among, the prevalence of mild-moderate and severe

hypoglycemia episodes was 50 and 21%, respectively. Similarly, among patients on the treatment of sulfonylurea, the prevalence of mild-moderate and severe hypoglycemia was 30 and 5%. It was also found 5% of prevalence among those who did not include sulfonylureas in the treatment regime [17].

The U.K. Hypoglycemia Study Group showed that patients with T2DM treated with insulin for < 2 years had a 7% prevalence of severe hypoglycemia compared to 25% in those treated with insulin for > 5 years.[18] This suggests that with greater duration of insulin treatment, the rate of hypoglycemic events increases. Hepburn et al.[19] showed severe hypoglycemic frequencies were similar in T1DM and T2DM when matched for the duration of insulin therapy. Thus, with longer duration of diabetes and progressive insulin deficiency in T2DM, the rate of iatrogenic hypoglycemia resembles that of T1DM.

The overall prevalence of T2DM is 20 times greater than that of T1DM.[20] T2DM is a progressive disease and most people with T2DM will ultimately become insulin dependent. As a result, most episodes of iatrogenic hypoglycemia, including severe hypoglycemia, occur in patients with T2DM.

RISK FACTORS FOR HYPOGLYCEMIA

Several factors influence an individual at risk (Table 1) for a hypoglycemic episode. These include a mismatch in the timing, amount, or type of insulin, skipping meals, eating small meal, irregular dietary pattern and lack of physical activity. Additional factors such as alcohol consumption, obesity, elderly people, liver disorders, renal disease, adrenal insufficiency (glucocorticoid or catecholamine deficiencies) and pituitary insufficiency and leukemia which increase the risk for hypoglycemia. Other factors at risk are those who have ingested medication salicylates and those who have surgery with general anesthesia, which places them in an altered state of consciousness and hypermetabolic state [15]. Another potential risk for hypoglycemia is the use of α -blocker and ACE inhibitor medication in cardiac and hypertensive patients which mask the

symptoms of hypoglycemia. α -Blockers inhibit the secretion of insulin and glycogenolysis due to diminishing of adrenergic counter regulation and also conceal the symptoms of catecholamine-mediated neurogenic hypoglycemia such as tremor, palpitation, hunger, irritability and confusion. However sweating remains unmasked and may be the only sign of patients treated with α -blockers [21]

PATOPHYSIOLOGY

The most metabolically active organ is brain and it is the first organ affected by lower blood glucose level. The brain requires continuous supply of oxygen and glucose to meet the needs of energy requirement as it does not store excess energy and derives almost all of its energy from aerobic oxidation of glucose. Hence brain cells are vulnerable to glucose deprivation and also cannot survive more than 5–6 min without glucose. The sequence of counter-regulatory response will play significant role when the blood glucose levels fall below 70 mg/dl to protect the brain from further deterioration of effects of hypoglycemia. Decline in Blood glucose levels below the physiological

range may trigger hierarchically organized sequence of responses in the non-diabetic individual [9, 22]. It includes release of neuroendocrine hormones or counter-regulatory or anti-insulin hormones, stimulation of the autonomic nervous system (ANS), and manifestation of neurogenic and neuroglycopenic symptoms. Pancreatic beta cells suppressed the insulin secretion when blood glucose levels declines within the physiological range results in reduction of peripheral glucose uptake and increase in hepatic glucose production to prevent true hypoglycemia. In further, declining intra-islet insulin plays an important role for the glucagon response to hypoglycemia by increase the release of glucagon by pancreatic alpha cells [8,23,24] and pancreatic polypeptide from the pancreas. Similarly catecholamines such as epinephrine secreted from the adrenal medullae and norepinephrine from sympathetic postganglionic nerve terminals and adrenal medulla. Cortisol from the adrenal cortex and growth hormone from the anterior pituitary gland also triggered when blood glucose level falls. The primary physiological fast acting hormones in response to hypoglycemia are glucagon and epinephrine. Glucagon hormones

Table 1 : Risk factors of hypoglycemia

Medical-related factors	Lifestyle-related factors
<ul style="list-style-type: none"> • Strict glycemic control • Previous history of severe hypoglycemia • Long duration of type 1 diabetes • Duration of insulin therapy in type 2 diabetes • Lipohypertrophy at injection sites • Impaired awareness of hypoglycemia • Severe hepatic dysfunction • Impaired renal function (including those patients requiring renal replacement therapy) • Sepsis • Inadequate treatment of previous hypoglycemia • Terminal illness • Cognitive dysfunction/dementia 	<ul style="list-style-type: none"> • Increased exercise (relative to usual) • Irregular lifestyle • Alcohol • Increasing age • Early pregnancy • Breast feeding • No or inadequate blood glucose monitoring

Reduced carbohydrate intake/absorption

- Food malabsorption, e.g., gastroenteritis, coeliac disease
- Bariatric surgery involving bowel resection

Other factors:

- Hypoglycemia unawareness
- Number of years since diabetes diagnosis
- Time since insulin initiated

enhance endogenous glucose production by the process of glycogenolysis and gluconeogenesis and generating glucose substrates such as lactate, pyruvate, alanine, and glycerol. In addition, epinephrine also has similar effects like glucagon in increase of endogenous glucose production and inhibition of utilization of glucose in the peripheral tissue and converts the gluconeogenic pathway. It can also stimulate net renal glucose production. However inhibition of insulin secretion is the primary physiological defense against decrease blood glucose and occurs at a plasma glucose concentration of less than 80 mg/dl. The response of sympathetic nervous system against hypoglycemia is activated by both circulating catecholamines and direct innervation results in increased fat metabolism of lipolysis in adipocytes which release free fatty acid. It is estimated that 25% of the total defense against hypoglycemia by the contribution of free fatty acid. Cortisol and growth hormone are metabolic defense which are released in response to prolonged hypoglycemia; but they have modest significant effect on glucose counterregulation during acute stage. The actions of these hormones are increasing glucose production and restraining glucose disposal after 4 h onset of hypoglycemia. It has only 20% of

counter-regulatory response compared to the action of epinephrine. If counter-regulatory mechanism fails to maintain the glucose homeostasis and blood glucose value of 3.0–3.5 mmol/l, may trigger the autonomic nervous system mediated warning symptoms such as sweating, palpitation and hunger to warn subjective awareness of hypoglycemia and provoke feeling of eating to improve blood glucose level. If not consume adequate glucose during this stage, central nervous deprives for glucose, neuroglycopenia develops and cognitive function declines. Counter-regulatory responses to hypoglycemia also referred to as glycemic thresholds and may be altered to higher plasma glucose levels following chronic hyperglycemia [25] or to lower plasma glucose levels following repeated hypoglycemia [6,26,27]. On the whole, the magnitude of counter-regulatory function is decrease with age 18 and is more obvious in male than in female [28].

CAUSES OF HYPOGLYCEMIA

Hypoglycemia is commonly occur in people with both type 1 and type 2 diabetes taking insulin or certain oral hypoglycemic agents. The common causes of hypoglycemia are:

Plasma glucose mg/dl (mmol/l)	Response	Function in hypoglycemia
80–85 (4.4–4.7)	Decrease in Insulin	First physiological defense against hypoglycemia. Primary glucose regulatory factor
65–70 (3.6–3.9)	Increase in Glucagon	Second physiological defense against hypoglycemia. Primary glucose counter-regulatory factor
65–70 (3.6–3.9)	Increase in Epinephrine	Third physiological defense against hypoglycemia. Critical when glucagon is deficient
65–70 (3.6–3.9)	Increase in Cortisol and growth hormone	Not critical, slower counter-regulatory factor
50–55 (2.8–3.1)	Neurogenic Symptoms	Prompt behavioral defense of food intake
<50 (2.8)	Neuroglycopenic symptoms	Compromised behavioral defense

TABLE 406-1 Causes of Hypoglycemia in Adults

III or Medicated Individual

1. Drugs
 - Insulin or insulin secretagogues
 - Alcohol
 - Others
2. Critical illness
 - Hepatic, renal, or cardiac failure
 - Sepsis
 - Inanition
3. Hormone deficiency
 - Cortisol
 - Growth hormone
 - Glucagon and epinephrine (in insulin-deficient diabetes)
4. Non-islet cell tumor (e.g., mesenchymal tumors)

Seemingly Well Individual

5. Endogenous hyperinsulinism
 - Insulinoma
 - Functional β-cell disorders (nesidioblastosis)
 - Noninsulinoma pancreateogenous hypoglycemia
 - Post-gastric bypass hypoglycemia
 - Insulin autoimmune hypoglycemia
 - Antibody to insulin
 - Antibody to insulin receptor
 - Insulin secretagogues
 - Other
6. Disorders of gluconeogenesis and fatty acid oxidation
7. Exercise
8. Accidental, surreptitious, or malicious hypoglycemia

Source : Modified with permission from PE Cryer et al : Evaluation and Management of adult hypoglycemic disorders : An endocrine Society clinical practice guideline. *J Clin endocrinol Metab* 94:709, 2009

Insulin and oral hypoglycemic agents Diabetes medications such as insulin and Sulfonylureas are the most common causes of hypoglycemia in diabetic subjects [29]. Of these, Insulin is a definite cause of low blood glucose. The long-acting sulfonylureas such as glibenclamide and chlorpropamide are associated with more severe hypoglycemia than the shorter-acting drugs [30]. Metformin was the most frequent used oral hypoglycemic agents (66.4%) followed by sulfonylurea and the most prevalent combination therapy was metformin/glibenclamide regimen (28.5%). 60.3% of the patients did not follow

regular blood glucose checkup [31]. Several reports reveal that various pharmacological agents like metformin, rosiglitazone, etc., which have wide ranging side effects, including weight gain, hypoglycemia and risk of coronary heart disease [32]. Occasionally episodes of hypoglycemia may occur with metformin, as the most commonly used anti-diabetic drug, due to an imbalance between food intake and dose of metformin [33].

Glucose-lowering agent	Relative risk of hypoglycemia
Alpha-glucosidase inhibitor	+
Bromocriptine	+
Colesevelam	+
DPP-4 inhibitor	+
GLP-1R agonist	+
Insulin	++++
Meglitinide	++
Metformin	+
Pramlintide	+
Sulfonylurea	+++
Thiazolidinedione	+

DPP-4, dipeptidyl peptidase-4; GLP-1R, glucagon-like peptide-1 receptor.

+, no hypoglycemia; ++, infrequent hypoglycemia; +++, occasional hypoglycemia; +++, frequent hypoglycemia

Food pattern Eating foods with less carbohydrate than usual without reducing the amount of insulin taken. Timing of insulin based on whether consumption of carbohydrates is from liquids or solids which can affect blood glucose levels. Liquids are absorbed much faster than solids, so timing the insulin dose to the absorption of glucose from foods. The composition of the meal contains the amount of fat, protein, and fiber which can also affect the absorption of carbohydrates.

Dietary habit If meal is skip or delay, blood glucose could drop too low. Hypoglycemia also can occur when asleep and have not eaten for several hours.

Drinking alcohol Alcohol consumption increase the insulin secretion and makes the liver not to release the glucose effectively into the blood circulation especially if have not eaten enough food within around 6 h and also makes more difficulty to generate new glucose by liver. Hypoglycemia occur overnight if fall asleep after consuming

alcohol without eating food among people with diabetes.

Physical activity Exercise has plays a vital role and has many potential health benefits. However the exercise can lower blood glucose by utilizing glucose for energy. The factors influencing exercise induce hypoglycemia are the intensity, timing of exercise and duration. Hypoglycemia can occur during, 1–2 h after, or up to 17 h after exercise. Endogenous insulin secretion is reduced up to 40–60% while doing moderate intensity exercise among non-diabetic individuals. Hence it is mandate that decrease insulin dose or increase glucose intake is recommended before, during or after exercise depending on the intensity of exercise to prevent exercise associated hypoglycemia. Additionally, recent studies have observed the cycle of counter-regulatory failure between exercise and hypoglycemia. Thus, subsequent two episodes of prolonged, moderate-intensity exercise can inhibit autonomic nervous system and neuroendocrine responses by 50%. Similarly, 40–50% of counter-regulatory responses reduced during two episodes of antecedent hypoglycemia due to subsequent exercise [34]. Hence, there is a greater risk of hypoglycemia during exercise among individuals who have had a previous episode of hypoglycemia. This may be prevented by adjusting pre-exercise insulin dose, and consuming appropriate amounts of glucose.

Potential causes of in-patient hypoglycemia

One of the most serious and common causes of inpatient hypoglycemia are insulin prescription errors including:

- Misreading poorly written prescriptions.
- Confusing the insulin name with the dose.

Inborn errors of metabolism causing hypoglycemia Non-diabetic hypoglycemia also results from inborn errors of metabolism. Such hypoglycemia most commonly occurs in infancy but can also occur in adulthood. Cases in adults can be classified into those resulting in fasting hypoglycemia, postprandial hypoglycemia, and exercise-induced hypoglycemia.

Fasting (postabsorptive) hypoglycemia It is rare; disorders of glycogenolysis can result in fasting hypoglycemia. These disorders include glycogen storage disease (GSD) of types 0, 1, 3, and 4 and Fanconi-Bickel syndrome.

Patients with GSD Type 1 and 3 characteristically have high blood lactate levels before and after meals, respectively. Both groups have hypertriglyceridemia, but ketones are high in GSD type 3. Defects in fatty acid oxidation also result in fasting hypoglycemia. These defects can include (1) defects in the carnitine cycle; (2) fatty-acid α -oxidation disorders; (3) electron transfer disturbances; and (4) ketogenesis disorders. Finally, defects in gluconeogenesis (fructose-1, 6-biphosphatase) have been reported to result in recurrent hypoglycemia and lactic acidosis.

Postprandial (reactive) hypoglycemia Inborn errors of metabolism resulting in postprandial hypoglycemia are also rare. These errors include (1) glucokinase, SUR1, and Kir6.2 potassium channel mutations; (2) congenital disorders of glycosylation; and (3) inherited fructose intolerance.

Exercise-induced hypoglycemia Exercise-induced hypoglycemia, by definition, follows exercise. It results in hyperinsulinemia caused by increased activity of monocarboxylate transporter 1 in α cells.

Accidental, surreptitious, or malicious hypoglycemia Hypoglycemia caused by endogenous hyperinsulinism due to functional α -cell disorders, insulinoma, or the insulin autoimmune syndrome is called as accidental, surreptitious, or malicious hypoglycemia. It may also occur by accidental administration of insulin, or accidental ingestion of an insulin secretagogue such as sulfonylurea because ingestion of an insulin secretagogue causes hypoglycemia with increased C-peptide levels and hypoglycemia caused by exogenous insulin with decrease C-peptide levels reflecting suppression of insulin secretion.

CLINICAL MANIFESTATIONS OF HYPOGLYCEMIA

Hypoglycemic symptoms may manifest as neurogenic (autonomic) symptoms and cholinergic-mediated symptoms. Low blood glucose level triggered the neurogenic symptoms by activating the autonomic nervous system which releases the catecholamines (norepinephrine and epinephrine) from the adrenal medullae and acetylcholine from postsynaptic sympathetic nerve endings. Elevated epinephrine levels leads the symptoms and signs of shakiness, palpitations, sweating, nervousness, anxiety, pupil dilation, dry mouth, pallor. The cholinergic-mediated symptoms are hunger, diaphoresis and paresthesia. However, only 20% of the total neurogenic symptom was found during hypoglycemia among epinephrine infusion in intensively and conventionally treated euglycemic type 1 diabetic individuals which indicates that the symptoms of hypoglycemic is multifocal and is mainly araised from efferent pathways of central nervous system [35].

Neuroglycopenic symptoms occur as a result of deprivation of glucose in the brain cells during hypoglycemia. Neuroglycopenic symptoms are very difficult to perceive by an individual rather it is most often recognized by family members, friends and bystanders. These symptoms include irritability, confusion, aphasia, paresthesias, ataxia, headache and the most severe symptoms are seizures stupor, coma, and even death. It can also include transient focal neurological deficits such as diplopia, hemiparesis.

Neurogenic and neuroglycopenic symptoms are manifested by the activation of the sympathoadrenal system and brain's glucose deprivation. The brain is continuously depends on a circulating glucose for energy and for cognitive function. If

Neurogenic / Autonomic		Neuroglycopenic
Adrenergic	Cholinergic	Headache
Palpitations	Diaphoresis	Visual changes
Anxiety/Nervousness	Hunger	Dizziness
Tremors/tremulousness	Paresthesias/tingling	Weakness
		Confusion
		Agitation
		Irritability
		Drowsiness/Lethargy
		Seizure
		Coma

blood glucose levels fall causes cognitive dysfunction [36]. The 11 most commonly reported symptoms were used to form the Edinburgh Hypoglycemia Scale [37].

DIAGNOSIS OF HYPOGLYCEMIA

History collection

- Physical examination Blood Glucose Levels
- Diagnostic investigation: It includes
- Glucose—fasting and postprandial blood glucose
- Complete blood count
- Insulin
- C-peptide
- Beta-hydroxybutyrate
- Proinsulin
- Antibodies for insulin and its receptors
- Sulfonylurea and meglitinide screen
- Electrolytes, BUN/Cr, UA
- liver function tests,
- cortisol and thyroid levels, growth hormone level
- Other tests: CT and MRI

Hypoglycemia is suspected in patients with typical symptoms; in the presence of confusion, an

Autonomic	Neuroglycopenic	General malaise
Sweating	Confusion	Headache
Palpitations	Drowsiness	Nausea
Shaking	Odd behavior	
Hunger	Speech difficulty	
	Incoordination	

altered level of consciousness, or a seizure; or in a clinical setting in which hypoglycemia is known to occur. Blood should be drawn, whenever possible, before the administration of glucose to allow documentation of a low plasma glucose concentration. Convincing documentation of hypoglycemia requires the fulfillment of Whipple's triad. Thus, the ideal time to measure the plasma glucose level is during a symptomatic episode. A normal glucose level excludes hypoglycemia as the cause of the symptoms. A low glucose level confirms that hypoglycemia is the cause of the symptoms, provided the latter resolve after the glucose level is raised. When the cause of the hypoglycemic episode is obscure, additional measurements—made while the glucose level is low and before treatment—should include plasma insulin, C-peptide, proinsulin, and α -hydroxybutyrate levels; also critical are screening for circulating oral hypoglycemic agents and assessment of symptoms before and after the plasma glucose concentration is raised.

TREATMENT OF HYPOGLYCEMIA

The aim of the treatment includes correction of glucose deficiency, prevent the complication associated with hypoglycemia and treat the underlying the cause.

- History collection and physical examination
- Check the blood glucose—capillary blood glucose
- Assess the mental status of the patient
- Access intravenous line if needed
- Monitor blood glucose level

People with diabetes should be treated for hypoglycemia at the ADA-recommended glycemic threshold of ≤ 70 mg/dl (3.9 mmol/l). [38] When the person is conscious and able to respond, a fast acting carbohydrate is the treatment of choice. This will provide the fastest and most reliable route for glucose levels to return to normal. Consumption of snacks high in fat (such as ice cream or chocolate), or protein (cheese) may delay the absorption of carbohydrate), [39] and it will take longer for plasma glucose levels to normalize.

Initially 15-20 grams of carbohydrate should be sufficient to raise blood glucose level without causing hyperglycemia.[40] Therefore the "rule of 15" is often recommended. Ingest 15 grams of glucose, and check plasma glucose after 15 minutes to make sure that the level is rising. If the glucose level is still low, then another 15-20 grams of carbohydrate should be ingested. The glycemic response to oral glucose is usually transient and lasts less than 2 hours if hypoglycemia is secondary to insulin.[41] Once the person is out of immediate danger from hypoglycemia after treatment with rapid acting carbohydrates, there should be some determination of the likelihood of recurrent symptoms. If the next meal is more than 2 hours away or if the symptoms occurred in the middle of the night it is recommended that the person have a long-acting carbohydrate with mixed nutrients such as milk, nuts, whole grains or fruits after the initial treatment to prevent recurrent symptoms.[40]

Patients on alpha glucosidase inhibitors (acarbose, miglitol, voglibose) should be treated with pure glucose (dextrose) because these medications slow the digestion of other carbohydrates thereby decreasing their efficacy to raise blood sugar effectively. With severe hypoglycemia, when the patient is incapable of ingesting glucose, injectable glucagon is the treatment of choice.[40] It is important for the friends/family to be able to recognize the signs of hypoglycemia and to administer glucagon. A glucagon injection increases blood glucose levels by stimulating hepatic glycogenolysis and gluconeogenesis. Dosing for children less than 20 kg is 0.5 mg or 20-30 mcg/kg/dose and for larger children and adults is 1 mg. It can be given intramuscularly (IM), subcutaneously (SQ) or intravenously (IV). It can be repeated in 20 minutes if needed but there is a high incidence of nausea and vomiting with rapid administration of high doses, especially via IV route.[40] The emergency medical system should always be contacted for severe hypoglycemia.

If the patient remains unresponsive or when medical personnel arrive, the standard therapy is

25 g of 50% glucose (D50W), if IV access is available.[40] In a hospital setting the standard parenteral therapy for hypoglycemia is IV glucose as 25 g of 50% glucose (dextrose). The glycemic response to IV glucose is transient and a subsequent glucose infusion is often required. Food should be given as soon as it is deemed safe for the patient to eat.

If there is no means to measure blood glucose in a comatose patient with diabetes, empirical treatment for hypoglycemia should be initiated. There is no efficacy or safety data for such a scenario.

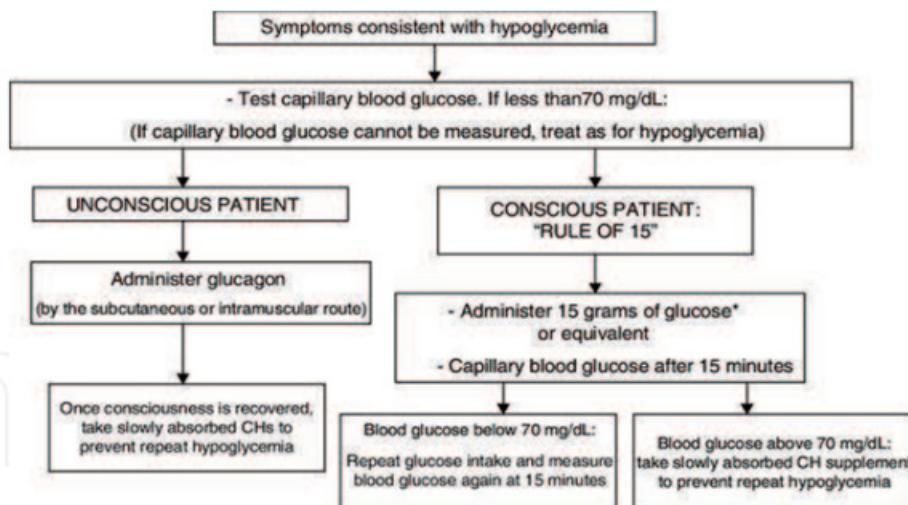
Management of non-diabetic hypoglycemia

Depend on the underlying etiology

- Discontinue the offending drugs or reduce their doses
- Treat the underlying critical illnesses
- Replace the cortisol and growth hormone if levels are deficient.
- Surgical, radiotherapeutic, or chemotherapeutic reduction of a non-islet cell tumor.
- Surgical resection of an insulinoma is curative
- Medical therapy with diazoxide or octreotide can be used if resection is not possible and in patient with a non-tumor beta cell tumor.

Health education

- Consult with a dietitian to develop or adjust meal plan to maintain consistency in carbohydrates at meals by calculating grams of carbohydrates so that plan for medication and/or insulin.
- Self-monitoring of blood glucose to detect the episodes of hypoglycemia at the earliest. Self-monitoring of blood glucose level should give an idea of what makes the blood glucose level drop.
- Do not skip meal and balance the meal plan with insulin or oral hypoglycemic agent.
- Quit alcohol and smoking.
- Maintain the body weight.
- Follow medication dose regularly.
- Avoidance of exercise while having the symptoms of hypoglycemia.
- Ingestion of carbohydrate especially rapidly absorbed glucose during the symptoms of hypoglycemia.
- Remember and follow rule of 15 which means 15 g of glucose raise 50 mg/dl in 15 min during hypoglycemia state.
- Intravenous glucose is the preferable treatment of severe hypoglycemia, particularly that caused by a sulfonylurea.



- Keeping the hypo box hypoglycemic kit which contains glucose, glucagon, juice, etc.
- Instructing the family members and care givers about usage this kit, check for expiry date and replacing the used content in the kit.
- Always carry the sweetener which contains easily absorbable simple sugar and identity card.
- Regular check-up and follow-up care.

COMPLICATIONS OF HYPOGLYCEMIA

Short-term risks of hypoglycemia include the dangerous situations that can arise while an individual is hypoglycemic, whether at home or at work (e.g. driving, operating machinery). In addition, prolonged coma is sometimes associated with transient neurological symptoms, such as paresis, convulsions and encephalopathy. The potential long-term complications of severe hypoglycemia are mild intellectual impairment and permanent neurologic sequelae, such as hemiparesis and pontine dysfunction. The latter are rare and have been reported only in case studies. Recurrent hypoglycemia may impair the individual's ability to sense subsequent hypoglycemia [28,42]. There is a clear association between severe hypoglycemia and cognitive disorders, but the nature of this relationship remains unclear. The person with cognitive disorders is at high risk of future severe hypoglycemic episodes, possibly because of medication errors [43,44,45]. Prospective studies have not found an association between intensive insulin therapy and cognitive function [46,47,48], or between severe hypoglycemia and future cognitive function [43,44]. Lowered cognitive performance appears to be more associated with the presence of microvascular complications or poor metabolic control than with the occurrence of severe hypoglycemic episodes [44,49]. In people with type 2 diabetes and established, or very high risk for, cardiovascular disease (CVD), there is a clear association between an increased mortality and severe hypoglycemia [50,51] and symptomatic hypoglycemia [52]. The mechanism

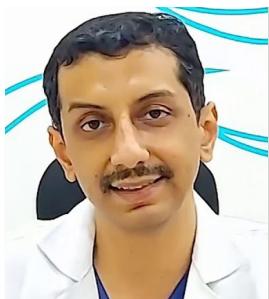
for this increase is not certain. Acute hypoglycemia is proinflammatory, increases platelet activation and decreases fibrinolysis, leading to a prothrombotic state [53,54]. Hypoglycemia is associated with increased heart rate, systolic blood pressure (BP), myocardial contractility, stroke volume and cardiac output, and can induce ST- and T-wave changes with a lengthening of the QT interval (slower repolarization), which may increase the risk of arrhythmias [56-59]. However, severe hypoglycemia may also be a marker of vulnerability, without any direct causal contribution to the increased mortality [60]

PREVENTION OF HYPOGLYCEMIA

All patients should be taught to recognize the symptoms of hypoglycemia and how to treat it promptly and appropriately. Behaviors that predispose to hypoglycemia such as alcohol ingestion (by inhibiting gluconeogenesis), exercise or unusual exertion (by increasing glucose utilization by muscle), and skipped, irregular or inadequate meals, should be reviewed with the patient. Patients on insulin or insulin secretagogues as sulfonylureas/glinide drugs should be educated on the risk of hypoglycemia associated with these agents. Among oral agents for diabetes sulfonylureas pose the greatest threat and should be substituted if causing recurrent hypoglycemia. Glyburide(long-acting insulin secretagogue) and sliding scale insulin are both on the 2012 Beers list, which is a list of medications that should be avoided in the elderly population to reduce their exposure to potentially inappropriate medications. [61]

Patients on intensive insulin therapy should be taught to replace insulin physiologically by taking basal/long acting insulin along with meal insulin to reduce the risk of hypoglycemia. The importance of taking meal insulin in relation to the meals should be emphasized. Patients should be encouraged to learn carb counting to enable them to "match the insulin" to their meals. Rapid-acting insulin analogs(lispro, aspart, glulisine) are preferred over regular insulin to reduce the risk of interprandial hypoglycemia as basal insulin analogs (glargine, detemir) are preferred over NPH

to reduce the risk of nocturnal hypoglycemia.[10] For exercise-related hypoglycemia, patients should be advised to check their blood glucose before, during and after exercise. The signs and symptoms of hypoglycemia (sweaty, shaky, palpitations) may be more difficult to identify in conjunction with exercise. This underscores the importance of frequent glucose monitoring. In addition, those who are participating in endurance aerobic exercise may find that they can develop hypoglycemia up to six to eight hours after the bout of exercise. Vigilance in monitoring and intake of carbohydrates should be considered. Caloric intake is recommended before, during or after exercise to prevent hypoglycemia related to physical activity. Insulin dose should be adjusted for days of planned activity to avoid lows related to exercise. Glucose monitoring is the backbone of diabetes management, especially so in patients prone to hypoglycemia. A CGM (continuous glucose monitoring) device should be considered in patients with recurrent hypoglycemia or with hypoglycemia unawareness. Because CGM displays the direction and rate of change of blood glucose, patients can act proactively to avoid hypoglycemia.



Pediatric Cardiac Emergencies

Dr Supratim Sen

Senior Consultant Pediatric Cardiologist
SRCC Children's Hospital, Mumbai
supratim80@gmail.com

Introduction

Pediatric cardiac conditions are of a very different spectrum compared to adult cardiac ailments. Children may present with a variety of cardiac emergencies. The initial presentation might be to a nearby emergency room (ER) and the first assessment of these patients will often be done by a general pediatric or medical specialist. Hence, awareness of the common pediatric emergencies and an overview of their initial recognition, stabilization and management will help clinicians in suspecting, diagnosing and treating these conditions in a timely manner.

Table 1 is a list of common pediatric cardiac emergencies encountered in pediatric cardiac practice.

Table 1: Common Pediatric Cardiac emergencies¹

1. Cardiopulmonary arrest and Shock
2. Arrhythmias
3. Hypercyanotic (Tet) spells
4. Congestive Cardiac failure
5. Duct dependent lesions
6. Shunt or stent thrombosis
7. Pericardial tamponade
8. Pulmonary hypertensive crisis

The commonest underlying heart diseases in children are congenital heart defects (CHD). CHD is seen in 8-10 per 1000 live births. While children with CHD may be more at risk of acute decompensation and presenting to the emergency department, many of the conditions mentioned in Table 1 can also be seen in children with

structurally normal hearts. In this manuscript, we have mentioned the salient features and treatment options for these conditions

1. Cardiopulmonary Arrest and Shock

The detection and treatment of cardiopulmonary arrest and shock is standardized with the Pediatric Advanced life support guidelines by the Indian Academy of Pediatrics and American Heart Association.²

A child presenting in shock will have cold, clammy extremities and feeble peripheral pulses with associated tachycardia and hypotension. The general first line of management comprises obtaining intravenous access followed by fluid resuscitation. The initial fluid bolus is limited to 10-20 ml/kg, with assessment of fluid responsiveness and overload prior to subsequent boluses.² Thereafter, the patient may also need inotropic support to maintain adequate systemic blood pressure and perfusion.

Differentiation of hypovolemic/septic shock and cardiogenic shock

Patients with septic shock and cardiogenic shock secondary to viral myocarditis may have similar history of fever and worsening breathlessness.

While rapid fluid resuscitation may be beneficial in septic shock, a child with myocarditis should have careful fluid boluses limited to 5-10 ml/kg, with earlier initiation of inotropes and earlier progression to Extra Corporeal Membrane Oxygenation (ECMO) if indicated. Any arrhythmias noted on ECG should lead to suspicion of a primary cardiac condition such as myocarditis. The confirmatory differentiating investigation is often

a screening echocardiogram, as patients with viral myocarditis will have severe left ventricular dysfunction, while a patient with septic shock will have normal left ventricular systolic function.

2. Arrhythmias

An arrhythmia is an abnormality of the rhythm of the heart. Broadly, this is classified into two types:

- tachyarrhythmia or fast heart rate
- bradyarrhythmia or slow heart rate

Tachyarrhythmias again are broadly of two types depending on their site of origin: atrial or ventricular.

In the emergency department, by far the commonest cardiac emergency is a child presenting with palpitations. The diagnosis can immediately be made by connecting an ECG.

The common and relatively benign cause of palpitations is supraventricular tachycardia or SVT. This is a regular, narrow complex tachycardia where the ventricular rate is usually $> 200/\text{min}$.



Figure 1: SVT (AVRT)

SVT is a reentrant tachycardia, which can be of two types: AV reentrant tachycardia (AVRT), due to an accessory pathway, and AV nodal reentrant tachycardia (AVNRT).

Treatment of SVT

The drug of choice to terminate the SVT is intravenous Adenosine. Adenosine is given in a dose of 0.1-0.3 mg/kg as a rapid IV flush followed immediately by a 10 ml flush of normal saline. In older children and adults, the starting dose is 6 mg and maximum dose is 12 mg.

The second drug we commonly use in the ER setting if Adenosine does not terminate the SVT is intravenous Metoprolol, given in a dose of 0.1 mg/kg in 10 ml NS, slowly over 10 minutes.

Often, while the medication or the defibrillator is

being arranged to treat the SVT, a simple vagal maneuver such as applying an icepack to the forehead of the child, dunking the back of the head of a baby in water to initiate the diving reflex, or a Valsalva maneuver in an older child may suffice to revert the SVT to sinus rhythm.

Synchronized cardioversion with a dose of 0.5-2 J/kg is the treatment of choice in a hemodynamically unstable patients with SVT.

Ventricular tachycardia

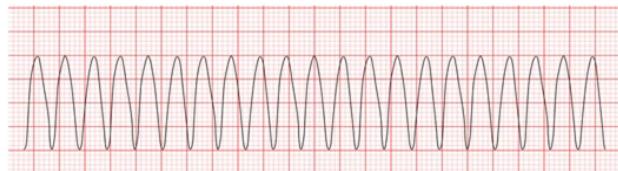


Figure 2A: monomorphic ventricular tachycardia

Ventricular tachycardias are wide complex tachycardias. Patients generally present in syncope or as an acute life-threatening event, as fast ventricular rates $> 300/\text{minute}$ are too high to maintain cardiac output and cerebral perfusion.

Treatment of VT

Although ventricular tachycardia can be treated by antiarrhythmic medications such as Lignocaine, Metoprolol or Amiodarone, in the emergency room setting, rapid reversal to sinus rhythm is essential for the patient's recovery and stabilization. Hence the first treatment of choice is synchronized cardioversion at 0.5 – 2 J/kg.

Medical conversion of ventricular tachycardia can be considered if a defibrillator is not available.

- I. Amiodarone loading dose is 5 mg/kg over 1 hour followed by maintenance dose of 5-10 mcg/kg/minute
- II. Lignocaine (Xylocard ™) is given in a dose of 1 mg/kg over 2 minutes, then 15-50 mcg/kg/min
- III. Beta-blockers such as Metoprolol (see above) and Esmolol- 0.5 mg/kg over 1 min and infusion rate of 25-300 mcg/kg/min

Polymorphic Ventricular Tachycardia: Torsades de pointes

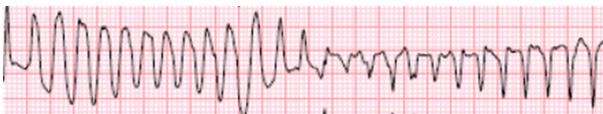


Figure 2B: polymorphic ventricular tachycardia

Polymorphic VT is classically seen in patients with long QT syndrome. The combination of congenital sensorineural deafness and long QT syndrome is an autosomal recessive condition known as Jervell and Lange-Nielson syndrome. Any patient with congenital deafness with episodes of syncope should be evaluated for long QT syndrome and polymorphic VT.

The treatment of polymorphic VT is with intravenous magnesium sulphate. The initial dose is 50% Magnesium sulfate 0.05-0.1 ml/kg IV, up to maximum 2 g (4 mL) per dose; dilute in 10 mL 5% dextrose, give IV or IO over 1 to 2 minutes in pulseless patients. In perfused patients, the dose is the same but is to be diluted in 10 to 50 mL 5% dextrose or NS and infused over 15 minutes (maximum 150 mg per minute).

Complete heart block

Patients with complete heart block, whether congenital or acquired, may present with syncope. The diagnosis can easily be made with an ECG. However, a first presentation to the emergency department with a slow heart rate of < 50/min will invariably lead to initiation of Cardiopulmonary Resuscitation by the emergency room physicians. Once complete heart block is diagnosed on ECG, emergency transvenous right ventricular pacing should be arranged via a temporary pacing lead inserted from the femoral vein. Some defibrillators also have the option of transcutaneous pacing with skin pacing pads. This can be done to maintain heart rate and cardiac output while the temporary pacing catheter is inserted. The definitive management of these patients is a permanent pacemaker.

Rarely, viral or COVID-19 myocarditis can present with transient complete heart block. These patients require temporary transvenous RV pacing for a few days while the inflammation is treated with IV steroids and IV immunoglobulin. The

rhythm in these patients may recover to sinus rhythm once the acute inflammation resolves.

Important points:

Attach an ECG monitor to all patients presenting to the ER with shock or breathlessness. This will help immediately diagnose arrhythmias.

3. Hypercyanotic (Tet) spells

Tetralogy of Fallot is the commonest cyanotic CHD. The primary defects in Tetralogy are a large malaligned ventricular septal defect and severe infundibular and valvar pulmonary stenosis. The malalignment of the VSD causes aortic override and the pulmonary stenosis causes right ventricular hypertrophy, which form the four morphological components of Tetralogy. In addition to TOF, many other cyanotic congenital heart defects including single ventricle hearts have VSD with pulmonary stenosis and are collectively termed as TOF physiology.

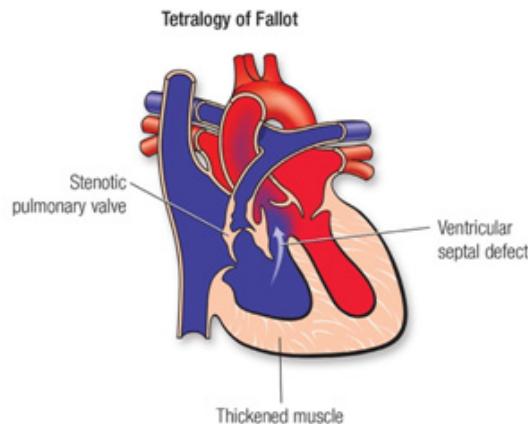


Figure 3: Schematic diagram of Tetralogy of Fallot

Tet Spells

The adequacy of pulmonary blood flow in TOF physiology determines the saturation of the patient. Sudden decrease in pulmonary blood flow due to infundibular spasm and sudden increase in the right to left shunting across the VSD due to a drop in systemic vascular resistance leads to hypoxia and desaturation, worsening metabolic acidosis and increase in the rate and depth of respiration (hyperpnoea). This constellation of features manifests as worsening

of cyanosis, or a cyanotic spell. All patients with TOF physiology can have a cyanotic spell.

If the spell is not controlled medically, the cyanosis and acidosis can progress to hypoxic seizures, loss of consciousness, stroke and even death. Spells are usually seen between 1-12 months age, most frequently between 2-6 months age.

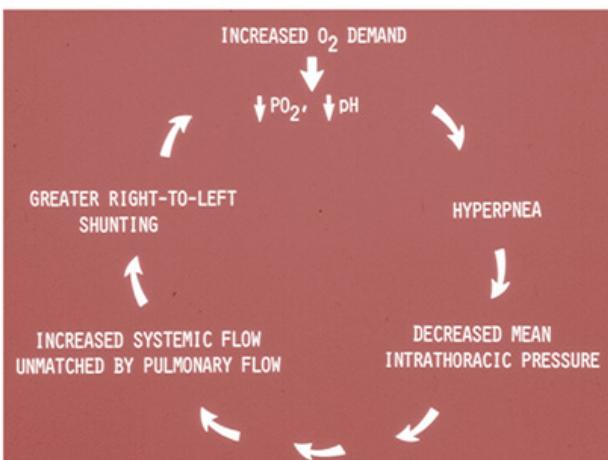


Figure 4: Mechanism of Cyanotic spells as proposed by Guntheroth¹

Treatment of Cyanotic Spells

- i. Put the baby in a knee-chest position. This increases the systemic resistance and decreases the right to left shunting across the VSD. This also allows pooling of the highly deoxygenated venous blood from the lower limbs below the abdomen and allows more oxygenated venous blood from the upper extremities to become the predominant venous return. Both these mechanisms improve the oxygenation of the blood in the central circulation.
- ii. Fluid bolus of normal saline- 10ml/kg- will increase the right ventricular preload and improve right ventricular output, especially in dehydrated patients.
- iii. Oxygen inhalation by nasal prongs should be started
- iv. Metabolic acidosis can be treated with intravenous sodium bicarbonate in a dose of 1 ml/kg given as 1:1 dilution with normal saline slowly over 20 minutes.

- v. IV/SC/IM Morphine in a dose of 0.1 mg/kg can be given to calm the patient, as sedation, and to treat the hyperpnoea by decreasing the respiratory drive.
- vi. Intravenous beta blockade with IV Propranolol or IV Metoprolol can be tried (see Metoprolol dose above).
- vii. Increasing the systemic vascular resistance with Phenylephrine or Noradrenaline may be tried.
- viii. Ventilation may sometimes be needed to terminate the cyanotic spell
- ix. If these above measures fail to terminate the cyanotic spell, rarely the patient may need emergency surgery with a BT shunt or intracardiac repair to treat the cyanosis.

4. Congestive Cardiac failure

Congestive cardiac or heart failure (CCF/CHF) is seen with functional or structural heart disease when the heart is unable to pump blood adequately to the systemic circulation to meet the systemic and metabolic demands. This can occur either with normal or depressed ventricular function. Children with left to right shunts such as ventricular septal defect, patent ductus arteriosus and atrioventricular canal defect have increased pulmonary blood flow with normal ventricular contractility and require additional cardiac output to maintain adequate systemic circulation. Similarly, patients with valve regurgitation such as mitral and aortic regurgitation may have normal ventricular function with features of CCF. Severe anemia can also present with CCF in the setting of normal ventricular function. Symptoms of CCF in children include failure to thrive, tachypnoea, respiratory distress and increased sweating.

In conditions such as myocarditis and dilated cardiomyopathy, the heart is structurally normal with decreased ventricular contractility. In addition to respiratory distress and tachypnoea, these patients may have cold clammy extremities and features similar to cardiogenic shock.

In the ER, a patient with an underlying cardiac disease in CCF may present with respiratory distress with signs of crepitations, hepatomegaly, chest indrawing, ascites, pedal edema and even desaturation.

Chest X-ray will confirm presence of pulmonary edema with cardiomegaly.

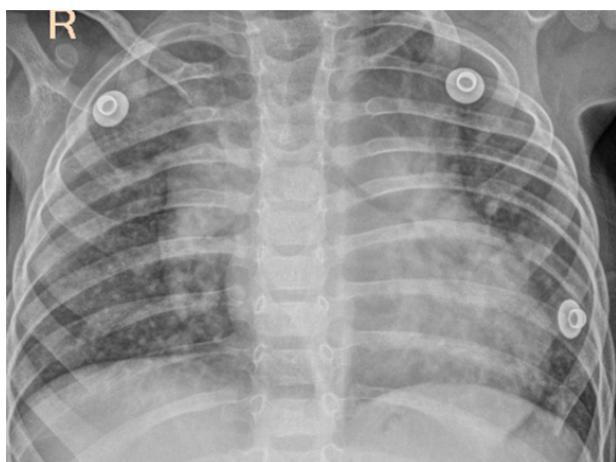


Figure 5: Cardiomegaly and pulmonary plethora in a patient with large VSD in CCF

Treatment of Congestive Cardiac Failure

- I. Diuresis with intravenous Frusemide is the first step to treat pulmonary edema. Frusemide is given intravenously in a dose of 1 mg/kg/dose
- II. Fluid resuscitation, if indicated, should be done carefully and gradually, and fluid boluses should be limited to 5 ml/kg
- III. Non-invasive ventilation with PEEP or invasive mechanical ventilation may be required for pulmonary edema with desaturation and respiratory distress
- IV. Inodilators such as Milrinone are helpful both in left to right shunts with CCF, by restricting the pulmonary overflow, and in ventricular dysfunction, by systemic vasodilation and afterload reduction.
- V. Sometimes, despite the above measures, the CCF may be refractory to medical treatment, and in these cases, the shunt lesion needs to be corrected by surgical or transcatheter intervention.

5. Recognition and emergency management of duct dependent lesions

All babies are born with a patent ductus arteriosus, which is essential for fetal circulation. The PDA will normally close spontaneously in the first 2 weeks of life. However, in some critical congenital heart defects, the PDA is essential for the survival of the baby till the time of corrective or palliative surgery. These conditions are known as duct dependent lesions.

Duct dependent lesions are of two types: duct dependent systemic circulation and duct dependent pulmonary circulation.

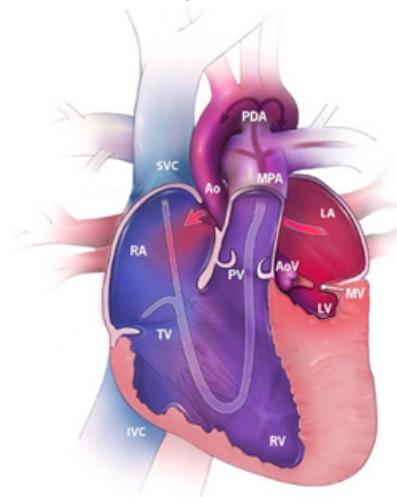


Figure 6A: Duct dependent systemic circulation-Hypoplastic Left Heart Syndrome

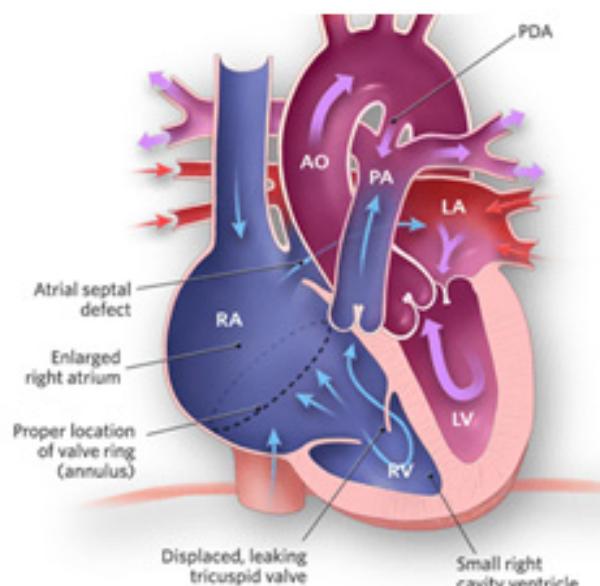


Figure 6B: Duct dependent pulmonary circulation with pulmonary atresia

In duct dependent systemic circulation, the PDA shunts right to left to perfuse the lower body. If the PDA were to close spontaneously, these patients would have absent lower limb pulses, acidosis and shock.

In duct dependent pulmonary circulation, the PDA shunts left to right and is the only source of pulmonary blood flow. If the PDA were to close spontaneously, these patients would have worsening cyanosis and desaturation.

In any baby presenting with sudden clinical deterioration within the first 2 weeks of life, the pediatrician should consider the possibility of duct dependent circulations with a closing PDA. These babies need to be urgently started on Prostaglandin E1 infusion in a dose of 100ng/kg/min to open the PDA. To maintain ductal patency, a dose of 10-20 ng/kg/min is adequate. Once the baby has been stabilized with prostaglandin, transfer can be arranged to a pediatric cardiac center for definitive or palliative surgery.

6. Shunt or stent thrombosis

In patients with duct dependent pulmonary circulation or TOF physiology, the first stage treatment is often a palliative procedure such as PDA stenting or BT shunt. These palliations are an additional source of pulmonary blood flow. To maintain patency of the stent or shunt, these patients are started on Aspirin +/- Clopidogrel. With a stent or shunt, the SpO₂ usually ranges between 75-85%.

Sometimes these patients might develop diarrhoea and vomiting with dehydration, and may also stop their Aspirin and Clopidogrel. These patients are then at risk of stent or shunt thrombosis and will present with sudden worsening of cyanosis and respiratory distress. On auscultation, the continuous murmur of the stent or shunt will not be audible if there is shunt/stent thrombosis.

Treatment of Shunt or Stent Thrombosis

This is a surgical emergency. If such a patient presents to a center without pediatric cardiac specialists, aggressive fluid resuscitation should be done to treat any dehydration. Heparin can be given in a dose of 100 U/kg as a bolus followed by maintenance infusion of 10-20 U/kg/hour. The patient should then be shifted to a cardiac center

as soon as possible. Thrombolysis should generally be avoided at peripheral centers, as that will preclude any emergency transcatheter or surgical intervention to reestablish pulmonary blood flow.

7. Pericardial tamponade ^{3,4}

Pericardial effusion can occur due to hypothyroidism, in systemic inflammatory conditions such as lupus and juvenile rheumatoid arthritis, post-infectious immune mediated conditions such as acute rheumatic fever, renal failure, viral pericarditis, bacterial/purulent pericarditis, tuberculous pericarditis and multisystem inflammatory syndrome in children after COVID-19. After cardiac surgery, pericardial inflammation can manifest with effusion. Malignancies of the pericardium can also present as pericardial effusion.

Pericardial tamponade is a condition where the pericardial effusion is large and affects the atrial and ventricular filling, and ventricular ejection. Clinical signs in these patients include tachycardia, raised jugular venous pressure, hypotension and narrow pulse pressure along with muffled heart sounds on auscultation. Sometimes patients can have signs of cardiogenic shock: cool extremities, peripheral cyanosis, hypotension and decreased urine output. Pulsus paradoxus is a clinical sign seen in cardiac tamponade, where weakening or disappearance of the pulse occurs during inspiration. On measuring blood pressure, pulsus paradoxus is defined as an exaggerated drop in systemic blood pressure of > 10 mmHg during inspiration.

ECG in these patients shows low voltage QRS complexes and electrical alternans, that is, beat to beat variation of QRS amplitude.

Treatment

Cardiac tamponade is an indication for emergency pericardiocentesis to relieve the intrapericardial pressure and to restore cardiac filling and cardiac output. Pericardiocentesis is done with echocardiographic guidance to minimize risks of puncturing the ventricular or atrial walls with the pericardiocentesis needle.

8. Acute Pulmonary Hypertensive Crisis

Pulmonary hypertension (PH) is a potentially life-threatening condition in pediatric cardiac practice.

Pulmonary hypertension is most commonly seen with large left to right shunts such as VSD and AV canal defects, and this is reversible if the lesion is treated in a timely manner. However, a significant proportion of patients have idiopathic PAH with structurally normal hearts and no parenchymal lung disease. These patients are treated with pulmonary vasodilators once the diagnosis has been made.

The first presentation of these patients may be an episode of syncope secondary to an acute pulmonary hypertensive crisis. There is a sudden surge in pulmonary vascular resistance, leading to right ventricular failure and the right ventricle is unable to eject blood into the lungs. Hence there is decreased pulmonary venous return to the left heart, and loss of cardiac output.

The patient may present with sudden rise in jugular venous pressure, desaturation, hypotension and syncope.

Pulmonary hypertensive crises should be treated by administering 100% oxygen, as oxygen is a potent vasodilator. Metabolic acidosis also needs to be corrected as acidosis is a pulmonary vasoconstrictor. If the pulmonary hypertensive crisis does not resolve, the patient may require intubation, ventilation, intravenous Sildenafil infusion and inhaled nitric oxide.

9. CHD presenting as an emergency

Critical congenital heart defects can present as a cardiac emergency. While these can only be treated at cardiac centers, correctly diagnosing a critically ill patient as a congenital heart defect is the essential first step towards an emergency pediatric cardiac evaluation, transfer to a cardiac center and timely cardiac intervention.

Here are a few examples of initial presentations of undiagnosed critical CHD:

- I. Critical aortic stenosis presents as shock with an ejection systolic murmur. These patients need emergency balloon aortic valvotomy.
- II. Critical pulmonary stenosis presents as cyanosis with an ejection systolic murmur. These patients need to be started on Prostaglandin E1 infusion followed by emergency balloon pulmonary valvotomy.
- III. Critical coarctation presents as shock with decreased lower body perfusion. These

patients are started on Prostaglandin E1 infusion and then undergo surgical arch repair or balloon dilation.

- IV. Obstructed TAPVC presents as cyanosis with respiratory distress. These patients need to undergo emergency TAPVC repair.
- V. Transposition of great arteries with intact ventricular septum may present as severe cyanosis. These patients need to undergo early arterial switch operation. If there is no nearby cardiac center, emergency balloon atrial septostomy under echocardiography guidance is a useful procedure for emergency stabilization of these babies prior to transfer to a cardiac center.

Conclusion

Pediatric cardiac emergencies can have varied presentations and can be potentially life threatening. However, correct clinical suspicion and timely diagnosis are the first step in their management, and with early institution of treatment, most of these conditions have good outcomes. General principles of Pediatric Advanced Life Support including establishment and maintenance of airway, breathing and circulation should be used as first line therapy for these patients. Additionally, early ECG monitoring and checking of SpO₂ along with checking all peripheral pulses are important aspects of the initial clinical assessment of these patients and are extremely helpful in correctly diagnosing the etiology of the pediatric cardiac emergency.

References

1. Yates MC, Rao SP. Pediatric Cardiac Emergencies. Emergency Med 2013; 3: 164.
2. Randhawa MS, Revaiah VC, Jayashree M. AHA Pediatric Advanced Life Support Update 2020 - "More Breaths, Less Fluids, and a Focus on Recovery". Indian Pediatr. 2021 Mar 15;58(3):273-278.
3. Borlaug BA. Pulsus paradoxus in pericardial disease. In: UpToDate, Post, LeWinter M (Ed), UpToDate, Waltham, MA, 2021.
4. Hoit BD. Cardiac Tamponade. In: UpToDate, Post, Gersh BJ, Hoekstra J (Eds), UpToDate, Waltham, MA, 2022.



Management of Upper GI Bleed

Dr R Kannan

Dept of Surgery, MGMC RI ,
Puducherry

Upper Gastro Intestinal Bleeding remains the most common Gastro - intestinal emergency.

In western countries, it is the cause of 50-100 hospital admissions per 1,00,000 population each year in the UK.

Upper GI Bleeding is the bleeding occurring before the duodeno jejunal junction. Most common causes are esophageal varices and peptic ulcer.

NON VARICEAL BLEEDING

AETIOLOGY

Common	Uncommon
Duodenal Ulcer	Gastric Ulcer
Angiodysplasia	Dieulafoy lesion
Oesophagitis	Gastric Antral Vascular Ectasia (GAVE)
Mallory -Weiss tear	Haemobilia

Peptic ulcer accounts for 30 to 60% of all episodes of upper gastrointestinal bleeding. 15-20% of patients with ulcers experience haemorrhage, the annual risk being 4%. Most peptic ulcers are caused by Helicobacter pylori infection or NSAID usage. NSAID usage accounts for 22 - 31% of all ulcer bleeds in elderly patients.

Adverse clinical prognostic factors in acute Upper GI Bleed

- Age more than 60 yrs
- Severe co- morbid medical (or) surgical illness
- Recurrent Bleeding
- Persistent Hypotension

- Severe coagulopathy (or) thrombocytopenia.

Causes:

1. Oesophageal causes

- Reflux oesophagitis
- Mallory-Weiss syndrome
- Oesophageal varices
- Cancer of oesophagus, leiomyoma oesophagus

2. Gastric causes

- Gastric ulcer
- Gastric varices
- Acute erosive gastritis
- Gastric cancer
- Stomal tumours-GIST
- Lymphoma
- Arteriovenous malformation
- Gastric polyp
- Dieulafoy vascular malformation
- Gastric antral vascular ectasia (GAVE)

3. Duodenal causes

- Duodenal ulcer
- Arteriovenous malformation
- Duodenal carcinoma
- Aortoduodenal fistula diverticulae
- Polyps

4. Other rare causes

- Purpura
- Haemophilia
- Haemobilia

- Pseudoaneurysms due to acute pancreatitis.

Diagnosis:

In the pre endoscopy era contrast study using barium used to be the main diagnostic modality. Currently Upper GI endoscopy is the gold standard in the diagnosis and also for planning therapy.

MANAGEMENT

Goals of management

The main goals are to achieve:

- 1) Hemodynamic stability
- 2) Stoppage of active bleeding
- 3) Prevention of recurrent bleeding

Achieving Hemodynamic stability:

This is achieved by initiating following measures:

- Starting IV line, preferably two lines, one line with wide bore needle.
- IV fluids with crystalloids and colloids
- Monitoring CVP / Vital signs
- Assessing cardiac status
- Monitoring urine output hourly.

Blood Transfusion:

It is essential to replace blood. Blood transfusion improves systemic oxygen delivery and improves coagulation.

Medical Measures:

Placement of nasogastric tube is debated. In an acute setting, if emergency endoscopy is being planned, placement of nasogastric tube may be deferred. Gastric lavage is not recommended since the lavage can dislodge the clots from the ulcer base.

Regarding pharmacotherapy earlier on antacids and H₂ Blockers were used. Mucosal protectives like sucralfate are used for upper GI bleeding due to gastric ulcer and gastric erosions. Currently high dose omeprazole is being used. 80mg of IV omeprazole as a initial dose and 8mg per hour subsequently helps in controlling the bleeding.

High dose of oral omeprazole ie. 40mg twice daily has been studied and accepted in the management of upper GI bleeding. Treatment of H.Pylori. Infection is also essential in the management of upper GI bleeding. The best approach is to test for H.Pylori before deciding on treatment.

Early Endoscopy:

Goal is to stop active bleeding and reduce the risk of recurrent bleeding.

- Early endoscopy and prompt discharge of low risk patient is safe and effective.
- Early endoscopy in high risk patients results in decreased transfusion requirement, rate of rebleeding and surgery.
- Helps in decreasing the period of hospital stay
- Early endoscopy is recommended immediately in all high risk patients and within 12-24 hours in all others.
- Emergency upper OGD is done to confirm the diagnosis. If the source cannot be detected due to large clots or massive bleeding, it can be repeated a few hours after a stomach wash and blood transfusion.
- Resuscitation is more important than an urgent endoscopy.
- Since elderly patients cannot tolerate shock well, decision to control bleeding surgically must be taken early.

Endoscopy in non Variceal Bleed :

- Establishes the cause of bleed
- Site and size of ulcers / stigmata of bleed
- To plan therapy
- Resumption of feeding
- Reduces the length of hospital stay.

II. NONSURGICAL TREATMENT

1. Laser coagulation

- It can arrest the bleeding without direct tissue contact.
- Nd:YAG laser has been used more commonly because it can penetrate tissue

more deeply compared to argon laser which penetrates very superficial tissues.

- The success rate of laser coagulation is around 80%.

2. Sclerotherapy

- Epinephrine (1: 10,000) arrests bleeding by vasoconstriction.
- 2% ethanolamine, a sclerosant causes dehydration and shrinkage of surrounding tissues.
- It also produces inflammation and thrombosis of the bleeding vessel.
- This is the most popular method. The success rate is around 80-90%. It is a cheap and easy treatment.

3. Haemoclip application

4. Bipolar electrocoagulation-failure rate is 50%

- Surgical eradication of H. pylori prevents rebleeding.

III. SURGICAL CONTROL OF BLEEDING PEPTIC ULCER

Indications

- Failure of endoscopic haemostasis prognostic factors are given below.
- Rebleeding in the hospital (rebleeding is more common in gastric ulcer patients).
- Bleeding requiring transfusion of more than 2000 ml blood in 24 hours (6 units).
- Elderly patients with rebleeding.
- Massive haemorrhage leading to shock or cardiovascular instability.
- Recurrent haemorrhage requiring hospitalisation

Types of surgery

- Surgery for bleeding duodenal ulcer
 - Laparotomy and anterior gastroduodenotomy.
 - Visualise the bleeding ulcer in the first part

of duodenum

- Under-running of the ulcer base by direct suture or 4 quadrant ligation of gastroduodenal artery by using nonabsorbable sutures.
- Gastroduodenotomy incision is converted into a pyloroplasty followed by vagotomy which completes the treatment.

2. Surgery for bleeding gastric ulcer (benign)

- Laparotomy, gastrotomy and visualise the bleeding ulcer.
- Under-running of the ulcer base. There are chances of rebleeding with this method.
- Partial gastrectomy is the best treatment provided general condition of the patient is good. Otherwise, local excision of the ulcer, vagotomy followed by GJ or pyloroplasty can also be done.
- Haemostatic methods currently employed include thermotherapy (heater probe, multipolar or bipolar electrocoagulation) as well as injection of ethanol or epinephrine solutions.
- When the bleeding is controlled, long-term medical therapy includes anti secretory agents, usually in the form of a proton pump inhibitor, in addition to testing for H. pylori with treatment if positive.
- If H. pylori is present, documentation of eradication should be performed after therapy.

Variceal Bleeding:

30 to 60 % of patients with Cirrhosis will have esophageal varices. Incidence of varices on follow up of patients with Cirrhosis is about 8% per annum. 10 to 20% increase in size of varices from small to large occurs in first year follow up. Risk factors for Bleeding are Child's class of Cirrhosis, size of varices and presence of Red Weal Marking

Natural History of Varices:

Patients with Cirrhosis but without varices will have 10 year survival upto 60%. Survival rate falls to 20% with large varices, which again falls to < 10% with single episode of Bleeding.

MANAGEMENT:

Pharmacotherapy:

Vasopressin causes splanchnic and systemic vasoconstriction. It achieves Haemostasis in upto 55% of cases. Side effects are myocardial infarction and cerebral Ischaemia. Terlipressin is more effective and less toxic. It is given in a bolus dose of 2mg IV and followed with 1mg 8'' hourly.

Octreotide and somatostatin helps in reduction of portal pressure. Somatostatin is administered as infusion 250 microgram hourly. Beta blockers reduce the risk of rebleeding by 40% and death by 20% . Nitrates alone are not useful but can be used in combination with beta Blockers.

Endotherapy:

Sclerotherapy

Sclerotherapy has been used to control variceal bleeding. commonly used sclerosants are sodium tetradecyl sulphate (STD) and Aethoxysclerol. Sclerosants are injected either intravariceally (or) Paravariceally. Complications noted are mediastinitis and pleural effusion.

Endoscopic Variceal Ligation -EVL:

EVL is more effective in obliteration of varices. Small number of treatment sessions are required when compared to sclerotherapy. Complications

are negligible.EVL is used in primary prophylaxis with a follow up ranging from 14 months to two years. Bleeding rates are three times higher in the untreated group. With EVL 5 to 8 fold reduction in variceal Hemorrhage related deaths. EVL is superior to sclerotherapy in terms of efficacy and complications. combination of beta blocker and EVL fares better than EVL alone.

Gastric fundal varices:

Fundal varices bleeds less frequently but more severely. Gastric fundal varices are classified as GOV, (varices in lesser curvature of stomach) Gov, when it involves fundus. IGV, when the gastric varices is Isolated to fundus. IG2. when the varices occurs any where other than fundus.

Management:

With variceal ligation rebleeding rates are upto 18.5%. Sclerotherapy controls the bleeding in 40 to 100% of patients but there is high recurrence rate of rebleeding and frequent surgical intervention required. Injection with glue(cyanoacrylate) has become gold standard in the management of gastric fundal variceal Bleeding.

Success rates achieved are upto 90 to 95% with less rebleeding rates.

Side effects are embolism, portal vein thrombosis and splenic infarction. In uncontrollable variceal Bleeding, we will have to consider TIPPS-(Tranjugular, Intrahepatic porta systemic shunt). TIPPS is more effective than endotherapy and pharmacotherapy in preventing rebleeding. It is associated with risk of encephalopathy and does not increase the survival.



Fulminant Hepatic Failure

Dr Neelam Mohan

Director

drneelam@yahoo.com

Department of Pediatric Gastroenterology, Hepatology and Liver transplantation,
Medanta- The Medicity, Gurugram, Haryana

Dr Saini Kumar Bana

Senior Resident

Saini.kumar24@gmail.com

INTRODUCTION

Acute liver failure (ALF) or fulminant hepatic failure (FHF) is a rapidly progressive clinical syndrome characterized by sudden acute deterioration of liver functions with significant morbidity and mortality. FHF is a medical emergency and carries a very high mortality of around 85% without liver transplantation.^{1,2} Mortality in ALF is related to multiorgan dysfunction, cerebral edema, sepsis, coagulopathy and bleeds. Management is reliant upon intensive clinical care and support, often provided by the collaborative efforts of hepatologists, critical care specialists, and liver transplant surgeons. Orthotopic liver transplantation (OLT) is a substantial advancement in the management of ALF and provides definite treatment.

Definition of ALF or FHF

In the setting of acute hepatitis, ALF implies that there is evidence of abnormal liver synthetic function (international normalized ratio: INR > 1.5) and the development of altered mental status (hepatocentral nervous system encephalopathy) within 26 weeks of the onset of illness in a patient without a history of liver disease. Nonetheless, although the definition of ALF excludes the presence of previous underlying liver disease, there are some exceptions to this definition: an acute presentation of Wilson's disease, autoimmune hepatitis (AIH), Budd-Chiari syndrome or hepatitis B virus infection.

The PALF Study Group (PALFSG) defines ALF in children as follows:

All the 3 components are required to meet the criteria for ALF.

- Acute onset of liver disease without evidence of chronic liver disease.
- Biochemical evidence of severe liver injury Coagulopathy not corrected by vitamin K
- Prothrombin time (PT) 15 s or INR 1.5 with evidence of hepatic encephalopathy or PT 20 s or INR >2 with or without encephalopathy

Etiology of acute liver failure

FHF affects children worldwide and the etiology remains age and region dependent, with viral hepatitis probably the most common identifiable cause in all age groups overall.

In infants, metabolic disease is the most frequent cause of ALF, whereas in children, viral hepatitis (in developing countries) or drug induced ALF (in North America and United Kingdom) is most frequently seen.³ GALD-NH (Gestational alloimmune liver disease - Neonatal hemochromatosis) is the most common cause of liver failure in neonatal period followed by infective and metabolic liver disease. Common etiologies for ALF in children are mentioned in table 1.

In adults, the common etiologies for FHF are : Acetaminophen intoxication, Viral etiologies (Hepatitis B virus, Hepatitis C virus, Hepatitis E virus, Cytomegalovirus, Epstein Barr virus Herpes simplex virus, Varicella zoster virus), autoimmune hepatitis , Wilson's disease , Budd-Chiari syndrome , Drug-induced liver injury (idiosyncratic reaction), Amanita phalloides intoxication ,Acute fatty liver of pregnancy, HELLP syndrome, Ischaemic hepatitis.

Clinical symptoms and signs

The clinical presentation of PALF varies based on age and etiology. Frequently, a prodromal phase with non-specific symptoms of fatigue, malaise, nausea, and abdominal pain is elicited.⁴ (Table 4)

A history of fever is occasionally reported. Identification of liver disease may not occur until jaundice becomes clinically apparent, or clinical decline prompts liver function testing. While a precise timeline of symptoms is important, it is often difficult to ascertain, and may not correlate with onset of liver injury.

Physical examination

Physical examination may be normal in the early stages of ALF; however, initial, and serial

neurological examinations should be performed to assess mental (e.g., attentiveness, confusion, orientation) and neurological (e.g., brisk reflexes, Babinski sign) signs of HE.

Signs on initial examination suggestive of an underlying chronic liver disease are essential. Few clinical signs which are suggestive of underlying CLD are growth failure, dysmorphic features, hepatosplenomegaly suggestive of portal hypertension, ascites, digital clubbing, rachitic rosary, xanthomas, abdominal varices or spider angiomas.

Diagnosis

Diagnosis is established by a combination of clinical and biochemical features and specific diagnostic tests (Table 2,3).

Table 1 : Etiology of ALF in older children

Infective	Viral Viral hepatitis A, B, B + D, E Non-A-E hepatitis (seronegative hepatitis) Adenovirus, Epstein-Barr virus, Cytomegalovirus, Echoavirus, varicella, Measles, Yellow fever rarely, Lassa, Ebola, Marburg virus, Dengue, Toga virus Bacterial Salmonellosis, Tuberculosis, septicaemia Others: Malaria, Bartonella, Leptospirosis
Drugs	Dose-dependent Acetaminophen, Halothane Idiosyncratic reaction Isoniazid, Nonsteroidal anti-inflammatory drugs Phenytoin, Sodium valproate, Carbamazepine, Ecstasy, Antibiotics (penicillin, erythromycin, tetracyclines, sulphonamides, quinolones) Allopurinol, Propylthiouracil, Amiodarone, Ketoconazole, Antiretroviral drugs Synergistic drug interactions Isoniazid + rifampicinTrimethoprim + sulfamethoxazoleBarbiturates + acetaminophenAmoxycillin + clavulanic acid
Toxin	Amanita phalloides (mushroom poisoning), Herbal medicines, Carbon tetrachloride, yellow phosphorus, Industrial solvents, Chlorobenzenes
Metabolic	Wilson's disease, hereditary fructose intolerance, alpha-1 antitrypsin deficiency, Fatty acid oxidation defects, urea cycle disorder
Autoimmune	Type 1 autoimmune hepatitis, type 2 autoimmune hepatitis, Giant cell hepatitis with Coombs-positive haemolytic anemia
Vascular	Budd-Chiari syndrome, Acute circulatory failure, Heatstroke, Acute cardiac failure Cardiomyopathies
Infiltrative	Leukemia, Lymphoma, HLH

Table 2: General laboratory investigations

Systems	Laboratory investigations
Hematological	Complete blood cell count with plateletsPT - International normalized ratio, aPTTfibrinogen, D – dimer, blood group, cross match
Electrolytes	Blood glucose, lactate, arterial ammonia, serum osmolarity. Blood gas with pH, sodium, potassium, calcium, magnesium, bicarbonate, Creatinine
Sepsis	Procalcitonin, urinalysis and microscopic analysis, blood cultures , urine cultures, tracheal cultures (if intubated)
Imaging and other testing	Chest radiograph, electrocardiogram, abdominal ultrasound with doppler study of the liver
CNS	EEG, BIS, ICP monitor ?

BIS indicates bispectral index; ICP, intracranial pressure

Table 3: Specific diagnostic tests to evaluate etiology of acute liver failure

Cause	Test
Hepatitis A infection	Anti-HAV antibody (IgM)
Hepatitis B infection	HbsAg, Anti-core antibody (HbcAb IgM)
Hepatitis D infection	Anti-hepatitis D virus antibody (IgM)
Hepatitis C infection	Anti-hepatitis C virus antibody (IgM)
Other Infections	HHV-1, 2, ; CMV; EBV; VZV; echovirus; parvovirus B19; malaria; dengue; leptospirosis
Autoimmune hepatitis	Autoantibodies ANA, ASMA, anti-LKM1, immunoglobulins IgG
Haemophagocytic Lymphohistiocytosis	Bone marrow aspiration (typical cells), raised ferritin , raised TGs, low/absent NK cell activity
Neonatal haemochromatosis / Congenital allo immune hepatitis	Buccal mucosal biopsy, raised ferritin, high transferrin saturation
Veno-occlusive disease	/Malignancies Doppler ultrasonography/ venography Imaging (computed tomography/ magnetic resonance imaging) and histology
Toxicology screen and drug panel	Acetaminophen, Opiates, Barbiturates, Cocaine, Alcohol

Metabolic Liver Disease	
Galactosaemia	Galactose-1-phosphate uridyl transferase assay (provided child not received blood transfusion in last 3 months)
Tyrosinaemia	Urinary succinylacetone
Wilson's disease	Urinary copper ($>100\text{ microgm/day}$), Kayser– Fleischer ring, Coombs negative haemolytic anaemia, low serum ceruloplasmin ($<10\text{ mg/dL}$)
Urea Cycle Defect (UCD)	Plasma aminoacidogram, Orotic acid estimation in urine to diagnose supplementation OTC deficiency
Fatty Acid Oxidation Defect	Carnitine - acyl carnitine profile
Mitochondrial hepatopathies	Muscle and liver biopsies for quantitative assay of respiratory chain enzymes, tandem mass spectroscopy

Management

FHF involves multiple organ systems. There is no specific therapy and liver transplantation is the definite modality for treatment. Management therefore is directed towards organ supportive care, prevention and treatment of complications, early consideration for liver transplantation. With advances in critical care medicine and liver transplantation mortality has considerably reduced.

General care

Management should be in an intensive care unit in an institution with an active transplant program. Priorities of intensive care management should include airway breathing and circulation. In patients with worsening encephalopathy (grade III, IV) and cerebral edema, increasing oxygen requirement, early acute respiratory distress syndrome (ARDS), or shock with or without multi-organ failure, endotracheal intubation and mechanical ventilation should be considered. For sedation, propofol/benzodiazepines are used, propofol has the added benefit of decreasing cerebral blood flow and lowering intracranial pressure.⁵

A central venous catheter will be required for assessment of central venous pressure and volume status. Use of a double lumen or preferably triple lumen catheter enables simultaneous

administration of blood products, intravenous fluids and drugs, and also makes blood sampling easy. An indwelling arterial line for measurement of blood pressure and for biochemical and acid-base monitoring is essential. A nasogastric tube is put in with regular gentle saline lavage to detect upper gastrointestinal bleed and to prevent aspiration. The urinary bladder is catheterized and strict output record maintained. Care should be taken for prevention of bed-sores. Baseline biochemical and other investigations are performed. Frequency of monitoring will depend on the severity of illness ranging from daily in mild cases to 4-6 hourly in patients with stage III and IV coma and include complete blood count, blood gases, electrolytes, aminotransferases and prothrombin time, plus daily monitoring of plasma creatinine, bilirubin and ammonia and chest X-ray to follow the ARDS and heart size. An abdominal ultrasound may indicate liver size and patency of hepatic and portal veins, particularly if liver transplantation is being considered. Vitamin K is given to all patients though may be avoided in G6PD deficient cases due to risk of hemolysis. The nursing of the patient should be in a quiet environment and one must avoid excessive stimulation and pain. Sedation should also be avoided. If the patient needs sedation he/she should be electively intubated for assisted ventilation.⁵

Fluid management

Both under and over-hydration are detrimental for patients with ALF, hence euolemia should be targeted. Hydration status is best monitored by central venous pressure. An accurate weight chart updated at least twice a day is also an acceptable surrogate. Urine output monitoring is essential to assess of hydration status and renal function of the patient.

Glucose

Nearly 40% of patients with ALF experience episodes of hypoglycemia due to increased plasma insulin levels as a consequence of reduced hepatic uptake and reduced gluconeogenesis. In patients with ALF, initial IV fluid should have at least 100 mg/ml of glucose (10%) to maintain euglycemia.⁶

Management of dyselectrolytemia

Hypokalemia

Hypokalaemia is a cause of metabolic alkalosis, which impairs ammonia detoxification, increases renal ammonia production, and leads to increased diffusion of ammonia across the blood-brain barrier. Studies have documented the potassium requirements in patients with ALF in the range of 3- 6 mEq/kg/day.⁶

Sodium

Hyponatremia is also relatively common in patients with ALF. Correlation between serum sodium and ICP has been demonstrated in various studies.

Studies have shown that infusion of hypertonic saline in patients with ALF results in a reduction of ICP and decreased vasopressor requirement. serum sodium level should be maintained between 140 and 145 mmol/L. Serum sodium levels more than 150 mmol/L may lead to osmotic cell damage, hence high levels should also be avoided.⁶

Management of coagulopathy

Deranged hepatic synthetic functions lead to

coagulopathy in ALF as measured by the prothrombin time (PT). However, despite the deranged PT/INR, clinically significant bleeding is rare, occurring in 5% and spontaneous intracranial bleed in 1%.⁷ The possible advantage of reduced bleeding by repletion of coagulation factors with fresh frozen plasma has not been established by clinical studies. Prophylactic FFP transfusion also carries a further disadvantage of volume overload, transfusion-associated lung injury, and hyperviscosity. Correction of coagulopathy is indicated only if the patient is already listed for transplant or prior to an invasive procedure such as insertion of a central line or ICP monitors.

Marked coagulopathy (INR > 7) should be corrected (10 ml/kg of FFP 6 hourly) to prevent the risk of bleeding particularly intracranial haemorrhage.¹⁶ Platelet transfusions should be used in patients with a platelet count of < 10,000 /mm³ or platelet count < 50,000/mm³ with associated bleeding.⁷

The gastrointestinal tract is the most common site for bleeding. Prophylactic histamine-2 blockers or proton pump inhibitors decrease the incidence of gastric bleeding; however, there is an increased risk of gastric colonization with their use. Sucralfate has the potential advantage of reducing gastric colonization and pulmonary infection by maintaining gastric acidity, but its efficacy in ALF is not well established.⁸

Hepatic Encephalopathy and Cerebral edema

Hepatic encephalopathy (HE) and cerebral edema represent two different neurological complications of acute liver failure. Careful observation is necessary to detect the onset and progression of HE.

The first line of treatment is to minimize aggravating conditions that can increase ICP. Therefore, any precipitating events that can result in hyperammonemia or raised ICP should be avoided. The usual standard line of treatment of encephalopathy in ALF is the following:

- Lowering endogenous nitrogen intake (by limiting bleeding the controlling infection)

or exogenous nitrogen intake (avoiding unjustified fresh frozen plasma administration) minimizing maintaining electrolytes, sugar and oxygenation.

- Raising the head end of bed to 20-30 degree, provided there is no shock. Avoidance of neck rotation additionally helps to reduce cerebral edema.⁹
- There is insufficient evidence for use of lactulose, lactitol, ornithine aspartate, rifaximin or sodium benzoate in ALF . Role of N-acetyl-cysteine in non paracetamol induced ALF is still controversial.¹⁰
- Hyperosmolar Therapy: They act by raising blood osmolarity, thereby reducing astrocyte swelling in brain. Mannitol is often the first-line therapy (2ml/kg/dose of 20% mannitol) and can be repeated as boluses. It is effective, if serial serum osmolality <320 mOsm/L. In patients with significant kidney injury or shock, its use is limited. Hypertonic saline can be used with a goal of achieving sodium of 145 to 155 mEq/L , provided serum osmolality remains below 360 mOsm/L.¹¹
- Spontaneous hyperventilation which is usual in patients with ALF should not be treated. However, prophylactic hyperventilation is not recommended in patients with ALF because vasoconstriction can reduce cerebral oxygen utilization. Acute transient hyperventilation (reduce PCO₂ 30 to 34 mm Hg for < 20 min) is however recommended as an emergency rescue therapy of patients with evidence of diencephalic herniation.
- Hypothermia (core body temperature 32 – 33°C) was reported to improve outcome in small case series, but was not found to confer benefit in 2 randomized trials.¹²
- Barbiturate coma- It is used to reduce brain metabolism, although incremental benefit is unclear if the patient is already in stage 4 encephalopathy with coma. Continuous EEG is recommended till burst-suppression is

achieved. Thiopental levels to be done frequently.

- Seizures: If seizure occurs in ALF, it has to be treated with phenytoin or levetiracetam as seizures cause spikes in ICP. But prophylactic anti-epileptics in ALF are not recommended.¹³
- Elective intubation and ventilation is undertaken when patients progress to grades II – III and become unmanageable. Propofol and fentanyl are suggested for analgesia and sedation. Positive end-expiratory pressure (PEEP) may increase ICP and should be used carefully.

More than 75%-80% of patients, especially in stage IV encephalopathy develop cerebral edema and raised intracranial pressure (ICP), the primary cause of death . Clinical signs of raised ICP include systemic hypertension, bradycardia, pupillary abnormalities, decerebrate posturing, epileptic form activity and brain stem respiratory patterns. However, most of these clinical signs are nonspecific and may develop in patients in hepatic grade IV encephalopathy without intracranial hypertension. Computerized tomography / Magnetic resonance imaging / Positron emission tomography are unreliable in diagnosis of intracranial hypertension in ALF patients. The most accurate method of diagnosis of intracranial hypertension is ICP monitoring.

Management of circulatory instability

Acute liver failure is associated with the release of cytokines, which leads to hyperdynamic circulation and low mean arterial blood pressure. After correcting the intravascular volume with crystalloids or colloids to maintain a central venous pressure between 6- 8 mmHg, vasoactive drugs may be required to correct the blood pressure to age-specific values. Norepinephrine has a more predictable effect in increasing cerebral perfusion in patients with traumatic brain injury and is preferred in adults with acute liver failure.¹⁴ Although, data in children are lacking these recommendations may be extrapolated to the paediatric population. An echocardiogram to

detect collapsibility of inferior vena cava may help tailor the fluid therapy.

Renal failure

Children with ALF may develop acute renal dysfunction due to tubular necrosis, acute hypovolemia, sepsis, drug toxicity and functional failure due to hepatorenal syndrome in cirrhotics. Ten to 17.5 % of children with acute liver failure require renal support.¹⁵

Hemodiafiltration or hemodialysis might be required to treat volume overload, oligo-anuria, metabolic disturbances, or for managing hyperammonemia. Continuous filtration or dialysis is associated with less hemodynamic instability and consequently less risk of aggravating latent or established encephalopathy than intermittent haemodialysis. In spite of the presence of coagulopathy, heparin requirements have been shown to be increased. Recently, prostacyclin infusion at a rate of 5 ng/kg/min has been found to be superior to heparin anticoagulation with respect to functional duration of the filters and the haemorrhagic complications.

Treatment of Infection

Patients with ALF are predisposed to bacterial and fungal infections. Some studies have documented the incidence of bacterial and fungal infections as high as 82% and 34% respectively.¹⁵ The most common site of sepsis is respiratory tract (47%), followed by the urinary tract (23%). Gram-positive bacteria have been isolated in about 70% of cases, 35% of these isolates being *S. aureus*. Renal failure, severe cholestasis, immunosuppressive therapy, and worsening coagulopathy are the high-risk factors for systemic fungal sepsis. The choice of systemic antifungal agents is determined by the local experience and as per institutional protocol.

There is a need for nutritional supplementation in ALF, because these patients are catabolic and enteral nutrition should be administered whenever possible, with higher caloric density feeds preferred. Normal protein intake recommended

till stage I & II encephalopathy and thereafter restriction (0.5 - 1 g/kg/day) is recommended. Metabolic liver disease presenting as ALF needs special nutrition plan, as diet modification in early stages can be life saving.

Specific Therapy

If any specific etiology for HE is found on etiological evaluation, specific therapy should be instituted. Specific therapy for some common disease processes is highlighted in **Table 4**.

Liver Assist Devices

Due to loss of functioning hepatocytes and kuffer cells in patients with ALF, impairment of synthetic, detoxifying, and bio-transformative activity of liver occurs. Several liver assist devices have been designed and studied as a mode of providing extracorporeal liver support. Liver support devices are classified as either cleansing devices or a bioartificial liver support systems. Cleansing devices (Charcoal hemoperfusion, biologic-DT) perform only the detoxifying function of the liver, whereas bio-artificial liver support systems (extracorporeal liver assist device, Molecular Adsorbent Recirculating System) have the advantage of providing synthetic and detoxifying properties.¹⁶

Plasmapheresis or Plasma Exchange (PE)

Adults case reports and case series have suggested PE can serve as a bridge to recovery or liver transplantation if applied on the first 3 days of admission to intensive care, by clearance of mediators, replacement of plasma derived factors and improving coagulation and other biochemical parameters.¹⁷

Liver transplantation

Liver transplantation is the only proven treatment that has improved the outcome in patients with ALF. According to the PALF study group, 45 % to 50% of cases with ALF in the USA, and 13% to 27% cases in Europe required liver transplantation.¹⁶

Table 4: Target specific therapy of underlying ALF

Cause	Treatment
Acetaminophen poisoning	Activated charcoal 1 g/kg orally
	N-acetylcysteine 150 mg/kg IV in 15 min, then maintenance dose 50 mg/kg over 4 hrs, followed by 100 mg/kg administered over 16 hrs
HSV	Acyclovir 10 mg/kg 8 hourly or 150 mg/ m ² /day IV
Neonatal hemochromatosis	Deferoxamine 30 mg/kg/day IV in 3 dosesSelenium 2-3 mcg/ kg/day IVN-acetyl-cysteine 140 mg/kg, then 70 mg/kg orally or IV tocopherol polyethylene glycol succinate 20 UI/kg/day orally
Mushroom poisoning	Penicillin G 300,000-1 million units/kg/day IVSilymarin 30-40 mg/ kg/day IV or orally
Hepatitis B	Interferon - á - 2b for children > 1 years of age and olderLamivudine or entecavir for children > 2 years of age and older
Autoimmunehepatitis	Methyl prednisolone 1-2 mg/kg IV (max 60mg)Azathioprine may be added to steroids.
Hemophagocytic lymphohistiocytosis	Corticosteroids Chemotherapy, Bone marrow transplantation

Selection for liver transplantation depends on the etiology of the disease, prognostic factors, presence or absence of multisystem disease and/or reversible brain damage. Perhaps the most frequently used criteria (**Table 5**) are those proposed by the King's College Group.¹⁸

Prognostic scoring systems like the King's College Hospital Criteria (KCHC) are routinely used in adult patients. Model for End-Stage Liver Disease (MELD) score have been validated and are routinely used in children >12 years. However, the sensitivity and positive predictive value for their use in PALF are low and do not reliably predict death in PALF

Pediatric End stage liver disease score (PELD) is used in children <12 years of age to predict mortality in children <12 years of age with chronic liver disease. Components of thisscore are bilirubin, albumin, INR, growth failure, and age <1 year. With a cut-off value of 33, the PELD score has a sensitivity (86%) and specificity (81%) for

poor outcome in children with chronic liver disease. However, its utility in predicting mortality in PALF has not been studied extensively.¹⁹

The revised Wilson Index (0–4 points) grades serum bilirubin, AST, INR, white blood cell count, and serum albumin. A score ≥11 is associated with a high probability of death without liver transplantation.²⁰

Liver transplantation could be:

1. Cadaveric
 - a. Whole graft—When the whole liver is used.
 - b. Split graft—When the donor liver is used for two recipients.
 - c. Reduced graft—When the donor liver is reduced to suit the size for recipient.
2. **Living related** —When a live donor gives part of his/ her liver to recipient.

Table 5: Prognostic indicators in ALF and criteria for liver transplantation

Scheme	Etiology of ALF	Criteria for liver transplantation
King's College	Acetaminophen induced Non-acetaminophen the etiology of the disease, prognostic factors, presence or absence of multisystem disease and/or reversible brain damage. Perhaps the most frequently used criteria (Table 11) are those proposed induced	Arterial pH < 7.3 OR all of the following 1) PT > 100 secs (INR > 6.5)2) Creatinine > 3.4 mg/dl3) Grade 3 or 4 encephalopathy PT > 100 secs (INR . 6.5) OR any 3 of the following :1) Non-A Non-B/drug/ halothane etiology 2) Jaundice to encephalopathy interval > 7 days3) Age < 10 or >40 years4) PT > 50 secs (INR> 3.5)5) Bilirubin > 17.4 mg/dL
Factor V (Clichy's)	Viral	Age < 30 years: factor V < 20% OR any age: factor V < 30% and grade 3/ 4 encephalopathy
Factor VIII/V ratio	Acetaminophen induced	Factor VIII/V ratio > 30
Liver biopsy	Mixed	Hepatocyte necrosis > 70%
Arterial phosphate	Acetaminophen induced	> 1.2 mmol/L
Arterial lactate	Acetaminophen induced	> 3.5 mmol/L
Arterial ammonia	Mixed	> 150-200 ?mol/L

Cadaveric transplants are very popular in the west while in countries like Japan, Korea, Hong-Kong and India, mostly living related liver transplantation are undertaken. In India, due to lack of awareness and shortage of cadaveric livers, living related liver transplantation is carried out for fulminant hepatic failure presently. In auxiliary liver transplantation, the liver graft is placed in the right upper quadrant beside the native liver. If the native liver recovers function, immunosuppression can be stopped. This is not suitable for transplantation for ALF secondary to metabolic liver disease, as these livers are unlikely to recover and there may be a risk of hepatoma in the cirrhotic liver.

Contraindications for liver transplantation are fixed and dilated pupil, uncontrolled sepsis, severe respiratory failure, irreversible cerebral edema with uncal herniation, and severe multisystem mitochondrial disease. Accelerating inotrope requirement, sepsis under treatment, cerebral

perfusion pressure < 40 mmHg for more than 2 hours, systemic disorders like HLH where LT is not curative, valproate toxicityare some of the relative contraindications for LT in PALF.

In author's centre (Dr Neelam Mohan), nearly 3800 LRLT have been performed, and more than 400 cases of paediatric living related liver transplantation have been performed. One third of these babies had weight less than 10 kg. Overall patient- and graft survival rates were 90.5% and 89%, respectively. Actuarial survival at 1 and 5 year was 94% and 87%, respectively. The survival was 100% for ALF.²¹

Conclusion

Fulminant hepatic failure is a heterogeneous condition with varied etiology, and requires extensive etiological workup, early referral, multidisciplinary management in a tertiary care centre. Timely institution of therapy to control

raised ICP is of utmost importance. Maintaining euvoolemia, treating the electrolyte dysbalance, associated infections are key steps of management. Importance should also be given to the nutritional status of the patient. Liver transplantation is the only effective treatment. Liver assist devices and hepatocyte transplant hold great potential of providing a bridge to transplant or avoiding it while the native liver regenerates.

REFERENCES

1. Dhawan A. Etiology and Prognosis of Acute Liver Failure in Children. *Liver Transplantation* 2008;14(Suppl 2):S80-4.
2. Cicocca M, Ramonet M, Cuarteola M, Lopez S, Caranden S, Alvarez F. Prognostic factors in paediatric acute liver failure. *Arch Dis Child* 2008;93:48-51
3. Squires RH Jr, Shneider BL, Bucuvalas J, et al. Acute liver failure in children: the first 348 patients in the pediatric acute liver failure study group. *J Pediatr* 2006;148:652-8.
4. Squires JE, McKiernan P, Squires RH. Acute liver failure: an update. *Clin Liver Dis* 2018;22:773-805.
5. Wijdicks EFM, Nyberg SL. Propofol to control intra-cranial pressure in fulminant hepatic failure. *Transplant Proc* 2002;34:1220-2.
6. Squires, James E.; Alonso, Estella M.". North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Position Paper on the Diagnosis and Management of Pediatric Acute Liver Failure. *Journal of Pediatric Gastroenterology and Nutrition*: January 2022 - Volume 74 - Issue 1 - p 138-158.
7. Stravitz RT, Kramer AH, Davern T, et al. Intensive care of patients with acute failure: recommendations of the U.S. Acute liver failure study group. *Crit Care Med* 2007;35:2498-508.
8. Macdougall BR, Bailey RJ, Williams R. H₂-receptor antagonists and antacids in the prevention of acute gastrointestinal haemorrhage in fulminant hepatic failure. Two controlled trials. *Lancet*. 1977;1(8012):617-619.
9. Dara N, Sayyari AA, Imanzadeh F. Hepatic Encephalopathy: Early Diagnosis in Pediatric Patients With Cirrhosis. *Iran J Child Neurol*. 2014 Winter; 8(1):1-11.
10. Squires RH, Dhawan A, Alonso E, et al. Intravenous N-acetylcysteine in pediatric patients with non-acetaminophen acute liver failure: a placebo-controlled clinical trial. *Hepatology*. 2013; 57: 1542-1549
11. Wendon J, Cordoba J, Dhawan A, et al. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. *J Hepatology* 2017;66(5): 1047 – 1081
12. Karvellas CJ, Todd Stravitz R, Battenhouse H, et al. Therapeutic hypothermia in acute liver failure: a multicenter retrospective cohort analysis. *Liver Transpl* 2015;21(1):4– 12.
13. Bhatia V, Batra Y, Acharya SK. Prophylactic phenytoin does not improve cerebral edema or survival in acute liver failure—a controlled clinical trial. *J Hepatol*. 2004; 41:89–96
14. Steiner LA, Johnston AJ, Czosnyka M, Chatfield DA, Salvador R, Coles JP, et al. Direct comparison of cerebrovascular effects of norepinephrine and dopamine in head-injured patients. *Crit Care Med*. 2004 Apr;32(4):1049-54.
15. Arya R, Gulati S, Deopujari S. Management of hepatic encephalopathy in children. *Postgrad Med J*. 2010 Jan;86(1011):34-41; quiz 40.
16. Jain V, Dhawan A. Prognostic modeling in pediatric acute liver failure. *Liver Transpl*. 2016 Oct;22(10):1418-30.

17. Larsen FS, Schmidt LE, Bernsmeier C, et al. High-volume plasma exchange in patients with acute liver failure: an open randomised controlled trial. *J Hepatol* 2016;64(1):69–78
18. McPhail MJ, Wenden JA, Bernal W. Meta-analysis of performance of King's College Hospital Criteria in prediction of outcome in non-paracetamol-induced acute liver failure. *J Hepatol.* 2010; 53:492-499
19. Chang CH, Bryce CL, Shneider BL, Yabes JG, Ren Y, Zenarosa GL, Tomko H, Donnell DM, Squires RH, Roberts MS. Accuracy of the Pediatric End-stage Liver Disease Score in Estimating Pretransplant Mortality Among Pediatric Liver Transplant Candidates. *JAMA Pediatr.* 2018 Nov 1;172(11):1070-1077.
20. Stankiewicz R, Patkowski W, Zieniewicz K. Diagnostic Dilemma and Treatment Outcome in Acute Liver Failure Due to Wilson's Disease. *Ann Transplant.* 2021 May 18;26:e930146.
21. Mohan N, Karkra S, Rastogi A, Dhaliwal MS, Raghunathan V, Goyal D, et al. Outcome of 200 Pediatric Living Donor Liver Transplantations in India. *Indian Pediatr.* 2017 Nov 15;54(11):913-918.



Thyroid crisis / Thyroid Storm / Thyrotoxic Crisis

Dr R Kannan

Dept of Surgery, MGMC RI ,
Puducherry

It is a rare but severe life-threatening complication of hyperthyroidism with acute hypermetabolic state induced by release of excessive thyroid hormones.

Crisis can be due to surgical or medical causes.

Causes:

- It occurs in a thyrotoxic patient inadequately prepared for thyroidectomy
- Thyrotoxic patient presents with crisis following an unrelated operation or stress.
- Other causes are –
- infection,
- trauma,
- pre-eclampsia,
- diabetic ketoacidosis,
- emergency surgery,
- stress,
- drugs like anticholinergics or antiadrenergic or NSAIDs or chemotherapy,
- diabetes mellitus.

CLINICAL FEATURES

- They present 12–24 hours after surgery; but on table also, it can occur occasionally.
- Hyperpyrexia ($> 41^{\circ}\text{C}$), severe dehydration, circulatory collapse, hypotension, palpitations, tachycardia, tachypnoea, hyperventilation, cardiac arrhythmias, cardiac failure.
- GI symptoms like vomiting, diarrhoea, jaundice.
- Restlessness, irritability, delirium, tremor, convulsions and coma can occur.

- Bailey's symptom complex of thyroid storm are – insomnia, anorexia, diarrhoea, vomiting, sweating, emotional instability, fever, tachycardia, aggravated toxic features, multiorgan dysfunction.
- Burch-Wartofsky score (1993) is used to identify or predict the thyroid storm using different parameters – score of below 25 excludes storm; score 25–45 suggests impending storm; more than 45 means thyroid storm.
- Death may ensue suddenly.

DIFFERENTIAL DIAGNOSIS are—

- malignant hyperpyrexia,
- septic shock,
- anxious status,
- cardiac disorders.

INVESTIGATIONS –

- Raised T3, T4,
- suppressed TSH,
- raised serum calcium,
- ECG and
- echocardiography shows changes,
- raised total count,
- altered liver function tests,
- arterial blood gas (ABG) shows changes;
- altered electrolytes.

TREATMENT

- **Supportive measures –**
- rehydration by proper fluid therapy,
- tepid sponging, cooling blankets,

- antipyretics like paracetamol IV infusion,
- glucocorticoids (Hydrocortisone 500 mg IV or dexamethasone injections),
- IV dextrose infusion as there is more metabolic demand,
- correction of electrolytes,
- treating cardiac arrhythmias,
- ICU care with ventilator support.
- Central line, CVP monitor, nasogastric tube, urinary catheter should be placed.

Antidiuretic drugs –

- Propranolol 80 mg orally or through nasogastric tube 6th hourly, or IV propranolol 1 mg IV in 10 minutes followed by 2 mg in 10 minutes as per need.
- When propranolol is contraindicated in asthma, heart block and failure, cardioselective beta blockers like atenolol, metoprolol can be used; esmolol IV loading dose as 500 ug/kg followed by 100 ug/kg minute infusion is also effective.
- Reserpine 500 ug/kg loading dose, then 5 ug/kg/minute; heart rate should be <100/minute.
- Thionamides – propylthiouracil (PTU) 200 mg 4th hourly or methimazole 20 mg 4th hourly or carbimazole is used.

Hepatotoxicity of PTU should be remembered.

- Iodide compounds – Lugol's iodide or potassium iodide is given one hour after intake of thionamides. 10–15 drops of Lugol's iodine 8th hourly is used or SSKI (saturated solution of potassium iodide) 5 drops 6th hourly is useful. Injection sodium iodide 1 gram IV is also used.
- Glucocorticoids – reduce the peripheral conversion of T4 to T3 and controls the shock. Hydrocortisone 5 mg/kg 6th hourly or dexamethasone 0.2 mg/kg/day are used.
- Bile acid suppressants to prevent reabsorption thyroid hormone from the gut – cholestyramine 4 grams 6th hourly. Iodinated radiocontrast dyes like iopanoic acid is also beneficial. Lithium carbonate 300 mg 6th hourly is also useful.
- Digitoxin, cardiac monitoring are crucial.
- Treating specific causes like diabetes, sepsis are important. Antibiotics, fluid and electrolyte management and monitoring is a must.
- Other measures—Haemodialysis, plasmapheresis, exchange transfusion, charcoal plasma perfusion are other methods used to control the storm.



IMA NATIONAL HEALTH SCHEME

Approved in Central Council 2014

Started in 2015



With the Aim to provide financial assistance to its member and his/her spouse, children and parents in the event of hospitalization for treatment, diagnosis and management of diseases

Benefits of the Scheme : Treatment cost above Rs. 5000/- to 2Lakhs will be covered per year -It will be increased to 2.5 to 3 lakhs as membership grows. Members and his dependents with pre-existing Diseases like Cancer, Cardiac, Life style diseases or any other Serious diseases are allowed to join this Scheme.

This provision makes IMA National Health Scheme unique from other schemes.

Fee Structure at the time of joining (First Year) Payment Chart of NHS according to age group

Payment chart at the Time of Joining

Age	AF	AMS	AFAC	Total
Less than 25yrs	1000	500	2500	4000
Above25 below35yrs	1000	500	3000	4500
35 to below 45yrs	1250	500	3000	4750
45yrs to 55yrs	1750	500	3000	5250
55 to below 60yrs	5000	500	5000	10500
60 to below 65yrs	7000	500	7000	14500
65yrs to below70yrs	8000	500	8000	16,500
70 to 80 yrs	10,000	500	10,000	20,500

Admission Fee is onetime Payment AMS & AFAC have to be paid every Year

Payment chart for renewal from 2nd Year onwards

Age	AF	AMS	AFAC	Total
Less than 25yrs	nil	500	2500	3000
Above25 below 35yrs	nil	500	3000	3500
35 to below 45yrs	nil	500	3000	3500
45yrs to below 55yrs	nil	500	3000	3500
55 to below 60yrs	nil	500	5000	5500
60 to below 65yrs	nil	500	7000	7500
65yrs to below 70yrs	nil	500	8000	8,500
70 to 80 yrs	nil	500	10,000	10,500

AMS &AFAC have to be paid every Year

Salient Features of IMA National Health Scheme (NHS)

1. In IMA NHS there is no escalation of annual premium amount even if the age progresses to the next slab for that particular insured amount. For example a person joining the scheme at the age of 25 years will be paying the same amount of Rs.3500/- till 55yrs as renewal fee per annum for an upper limit of 2 lakhs benefit.
2. Scrutinizing committee will examine the genuineness of the claim. 75% of the Total bill will be reimbursed to a maximum of 2 lakhs. Will be increased to 2.5-3lakhs
3. Allowed to join other insurance schemes and State Health Schemes. Total 3+2= 5 Lakhs benefits State HS+ National H.S
4. All pre-existing diseases are covered including Cancer and Organ Transplant
5. No medical screening test required for joining IMA National Health Scheme.
6. Member can join till the age of 80 years. It is the only Scheme which allows the IMA member and his family to join above the age of 65yrs .For all other schemes age limit is restricted to 65 yrs as upper limit
7. Immediate relatives of life members of IMA can also join.
8. Original bills are returned at request with Self addressed cover with stamp, and hence can be utilised for other insurance schemes for claim.
9. More than insurance companies, IMA NHS exist for the medical Fraternity and its family to provide financial help at the time of hospitalization.
10. Rs.50/- is eligible per member enrolled as promotional fee to local Branch or State branch or individual who promote the enrollment of NHS

Website : www.imanhs.com

It is an Additional Health Financial Scheme

Man by Professionals for profession. No Bureaucracy, so member friendly



INDIAN MEDICAL ASSOCIATION NATIONAL FAMILY WELFARE SCHEME

**A SCHEME EXCLUSIVELY FOR THE SCHEME MEMBER'S FAMILY AFTER DEATH &
FOR THE DISABLED, END STAGE DISEASED AND UNFIT TO PRACTICE**
E-mail: imanfws2018@gmail.com | www.nationalfamilywelfarescheme.com

Admission Fee :

Age	Admission Fee	1 st Annual Subscription Fee	Total Admission Fee
Below 30 Yrs	3,000	500	3,500
31-40 yrs	5,000	500	5,500
41-50 yrs	7,000	500	7,500
51-60 yrs	10,000	500	10,500
61-65yrs	20,000	500	20,500

Payment Mode : DD/Cheque in favour of "**IMA National Family Welfare Scheme**" Payable at Nedumangad, Thiruvananthapuram District.

Annual Subscription: Every year member should pay Rs.500 as annual subscription for 25 years. After that member will become Honorary Member and become eligible for all rights.

One Time Payment: By paying Rs.4,00,000 as Non refundable deposit the member will become life Member and become eligible for all rights and no need to pay other payments.

Member Benefits or Rights: • On the event of demise of a member : Fraternity Contribution RS.300/- (200/- to Fraternity Contribution & Rs.100/- to corpus fund) on the event of demise of any member (To a maximum of 50 deaths per year over which the Fraternity Contribution will be taken from the corpus fund) • Disabled or incapacitated Practitioner member will get a benefit from the Corpus Fund which will be judicially decided by the Management Committee.

LOCK IN PERIOD : • If the Age joining the scheme is below 50 years, the lock in period is 2 years. • If the Age of joining the scheme is above 50 years, the lock period is 3 years.

FOR MORE DETAILS: Log on to www.ima-india.org IMA National Family Welfare Scheme.



**I.M.A.
NATIONAL SOCIAL
SECURITY SCHEME**

IMA National Social Security Scheme (IMANSSS)

BENEFITS : On event of death (by any cause), rest of the members contribute a token share of Rs. 100-00, from which Rs. 70-00 is passed on to the nominee.

After 25 years of continuous membership, the member has not to contribute the same and the Fraternity Contribution (F.C.) will be paid to the nominee by the scheme.

BENEFIT FOR MEMBERS ENROLLED AFTER 19/07/2002 : For members enrolled after 19/07/2002, benefit of Fraternity Contribution of the scheme liable after completion of one year of membership of I.M.A. N.S.S.S. However nominee of member be entitled for such benefits if death of member occurs in accident event within one year of joining the scheme.

ELIGIBILITY : Any life member of I.M.A., up to age of 60 years residing in India is eligible to become a member of this scheme but members above the age of 40 years and below the age of 60 years, must be life member of IMA atleast for 3 years on the day of joining the scheme.

At present we have 19,070 members enrolled and paid Rs. 11,50,450.00 to the last deceased member's nominee.

Contact for Membership

Kindly contact on below email / call to get the membership information

Call us +91-79-26585430

E-mail: imansss1@gmail.com | Mail: contact@imansss.org | Website : www.imansss.org