Sepsis in Primary Care

Session Aims and Objectives

Aims: This session aims to provide an overview of how to identify sepsis and measures to take to manage the patient safely.

Objectives

- By the end of this session the delegate will:
- Have an understanding of causes of sepsis.
- Recognise at risk groups for sepsis
- Recognise red flag symptoms indicating possible sepsis
- Consider differentials in diagnosing sepsis
- Develop skills in management of persons with suspected sepsis

What is Sepsis

Sepsis is a syndrome defined as life-threatening organ dysfunction due to a dysregulated host response to infection.

Septic shock is a subset of sepsis, which describes circulatory, cellular, and metabolic abnormalities which are associated with a greater risk of mortality than sepsis alone.

It is thought to be a multifactorial response to an infecting pathogen that may be amplified by host factors (such as genetics, age, and co-morbidities), the pathogen (type, virulence, and burden), and the environment.

The most common sites of infection leading to sepsis are the respiratory, gastrointestinal, renal and genitourinary tracts

Prevalence

- The incidence of sepsis is increasing, which reflects an ageing populations with multiple co-morbidities, increased use of immunosuppressive drugs, increased antibiotic resistance, and increased awareness of the diagnosis
  - 250,000 cases of sepsis each year in the UK
  - A UK observational cohort study of 91 intensive care units (n = 56,673 adults) found that 27.1% of cases met sepsis criteria in the first 24 hours of admission
  - A review article states that estimates of sepsis prevalence range from 66 to 300 per 100,000 people in the developed world
  - A systematic review of 23 international observational epidemiological studies of neonates and children found an estimated incidence of 48 cases per 100,000 person-years.

Many patients are seen and managed for infections in primary care and only a very small fraction of these will have sepsis.

The skills and judgment of primary care clinicians are crucial and must be supported.

When primary care clinicians measure and record physiological observations and any alteration in mental state in patients in whom they suspect sepsis their diagnostic accuracy is improved.

Causes of Sepsis

- **The exact pathophysiology of sepsis is not known, but it is thought to be a multifactorial response to an infecting pathogen that may be amplified by host factors (such as genetics, age, and co-morbidities), the pathogen (type, virulence, and burden), and the environment.**
- The mechanism of cell injury is not fully understood, but it is theorized that immune and coagulation systems are switched on by infection and cause dysfunction of one or more organs with variable severity .
- It is thought this involves the early activation of both pro-inflammatory responses (leading to cellular and tissue damage) and anti-inflammatory responses (leading to immunosuppression). Resulting tissue hypoxia, mitochondrial dysfunction, macrovascular and microvascular dysfunction, and apoptosis are thought to be mediators of organ dysfunction

Causes of Sepsis

- The most common sites of infection leading to sepsis are the respiratory, gastrointestinal, renal and genitourinary tracts, as well as blood, skin, soft tissue, bone and joint sources

- Some studies cite an equal prevalence of Gram-positive and Gram-negative bacterial infections in people with sepsis, particularly *Staphylococcus aureus*, Pseudomonas species, and *Escherichia coli*
- In children, *Neisseria meningitides* and *Haemophilus influenzae* may also be involved
- Rarely, fungal, viral, or parasitic infections are causative
- In about one-third of people with sepsis, no causative pathogen is identified
- About 80% of hospital-treated sepsis cases originate from community-acquired infection [

Risk Factors

- Infants (under one year of age) and older people (over 75 years of age).
- People who are very frail.
- People who are immunocompromised due to a co-morbid condition (such as diabetes mellitus, HIV, cirrhosis, sickle cell disease, or asplenia).
- People who are immunosuppressed due to drug treatment (such as anticancer treatment, oral corticosteroids, or other immunosuppressive drugs).
- People who have had trauma, surgery, or other invasive procedures in the past six weeks.
- People with any breach of skin integrity (for example cuts, burns, blisters, or skin infections).
- People who misuse intravenous drugs or alcohol.
- People with indwelling lines or catheters.
- Women who are pregnant, are post-partum, or have had a termination of pregnancy or miscarriage in the past six weeks, including those who have:
  - Had a Caesarean section, forceps delivery or removal of retained products of conception.
  - Had prolonged rupture of membranes.
  - Or have been in close contact with people with group A streptococcal infection, for example, scarlet fever. Ongoing vaginal bleeding or an offensive vaginal discharge.

Complications of Sepsis

- **Sepsis is a leading cause of morbidity and mortality. Between one-fifth and one-half of sepsis survivors following hospital admission experience long-term sequelae ('Post-Sepsis Syndrome').**
- Death
- Recurrent infections may be due to immunosuppression from a persistent compensatory anti-inflammatory response
- Malnutrition
- Coagulopathy
- Physical impairments
- Encephalopathy and delirium
- Psychological sequelae

Remote Consultations

- In remote (non-face to face) assessments if a clinician suspects sepsis and has no access to physiological measurements they should arrange for the patient to attend a facility where these measurements can be recorded without delay.
- Where a primary care clinician suspects sepsis and the results of physiological observations suggest a risk of severe illness or death then the clinician should arrange urgent referral and transfer of the patient to an acute hospital for further assessment and treatment with minimal delay at the scene. Ambulance services are increasingly using NEWS as a way of translating physiological observations into a risk score and using this to pre-alert emergency departments when they are bringing acutely ill patients to hospitals.

NICE Recommendations

- NICE recommends that people with suspected sepsis are assessed for risk factors and then clinically using a structured set of observations (temperature, heart rate, respiratory rate, level of consciousness, oxygen saturation) to stratify risk of severe illness or death. The National Quality Board has encouraged further evaluation of NEWS in primary care.

When to suspect sepsis

- **Be aware that sepsis can be challenging to identify, as the clinical presentation is variable depending on the underlying cause and the person's age and co-morbidities.**
- Suspect sepsis in any person presenting with:
  - Symptoms or signs indicating possible infection causing significant illness or deterioration. This includes people who are deteriorating unexpectedly, or failing to improve as expected.
  - One or more risk factor(s) for sepsis, and who looks unwell.
  - Concern from a relative or carer that there is a change in appearance or behaviour.
- Be aware that:
  - People with sepsis may present with non-specific, non-localized clinical features, for example general malaise, agitation, or behavioural change.
  - People with sepsis may not present with a high temperature, and may present with hypothermia.
  - Sepsis may result from infection with almost any pathogen, therefore it may present with a wide range of clinical features depending on the site of infection and host response.
- Suspect neutropenic sepsis in any person who becomes unwell who is receiving anticancer treatment, and manage appropriately

Signs and Symptoms

- **Ask the person/carers about:**
  - Any recent fever or rigors.
  - Any symptoms suggesting specific infection, such as dysuria or productive cough.
  - Clinical features suggesting dehydration, such as reduced urine output in the past 18 hours.
  - Any altered behaviour, mental state, or cognition, such as not responding normally to social cues or waking only with prolonged stimulation, or new irritability (in children); new-onset confusion (in adults).
  - Any sudden change or deterioration in functional ability.
  - Possible risk factors for sepsis, including co-morbidities and drug treatments.
  - Possible risk factors for antibiotic resistance, such as recent or previous antibiotic therapy, previous hospital admissions, and residency in a care home, for example.
  - Immunization status (particularly in infants and young children).

Examination : Vital Signs

- General appearance, level of consciousness and cognition.
  - Cognitive assessment should include recognition of new-onset confusion, disorientation, and/or agitation. Temperature.
  - Fever is the most common presentation of sepsis. Do not use temperature as the sole predictor of sepsis, however, and do not rely on fever or hypothermia to rule sepsis in or out. Heart rate, respiratory rate and signs of respiratory distress, and blood pressure.
  - Signs of respiratory distress include nasal flaring, grunting, and apnoea in children less than 5 years of age.
  - Measure blood pressure in children under 12 years of age and oxygen saturation at any age in community settings, if facilities including a correctly-sized cuff or pulse oximeter are available, and taking a measurement does not cause a delay in assessment or treatment.
  - Hypotension is a presenting feature in 40% of people with sepsis, but be aware that a normal blood pressure does not exclude sepsis in children and young people.
- Capillary refill time and oxygen saturation (abnormal results may indicate poor peripheral perfusion

Examination : Skin

- Mottled or ashen skin; pallor or cyanosis of the skin, lips or tongue; cold peripheries.
- A non-blanching rash which may suggest meningococcal disease
- Weak high-pitched or continuous cry (in children under 5 years of age).
- Any breach of skin integrity (for example cuts, burns, or skin infections) or other skin signs suggesting infection, such as erythema, swelling or discharge at a surgical site, or wound breakdown. Dry mucous membranes or other signs of dehydration.
- The possible underlying source of infection

Risk Stratification Tools

- Royal College of Physicians National Early Warning Score (NEWS) 2
  for non-pregnant adults.
- NICE risk stratification tool for children under 5 years
  or
  UK Sepsis Trust GP Paediatric Sepsis decision support tool for children under 5 years
  .
- NICE risk stratification tool for children aged 5–11 years
  or
  UK Sepsis Trust GP Paediatric Sepsis decision support tool for children aged 5–11 years
  .
- NICE risk stratification tool for adults, children and young people aged 12 years and over
  or
  UK Sepsis Trust GP Sepsis decision support tool for non-pregnant adults and young people aged 12 years and over
  .
- UK Sepsis Trust GP Maternal Sepsis decision support tool for women who are pregnant or up to 6 weeks postpartum

NEWS

Six simple physiological parameters form the basis of the scoring system:

- respiration rate
- oxygen saturation
- systolic blood pressure
- pulse rate
- level of consciousness or new confusion*
- temperature.

**The patient has new-onset confusion, disorientation and/or agitation, where previously their mental state was normal – this may be subtle. The patient may respond to questions coherently, but there is some confusion, disorientation and/or agitation. This would score 3 or 4 on the GCS (rather than the normal 5 for verbal response), and scores 3 on the NEWS system.*

Differential Diagnosis

- Pulmonary embolism. Acute myocardial infarction
- Heart failure.
- Acute delirium.
- Acute pancreatitis.
- Diabetic ketoacidosis.
- Adrenal insufficiency.
- Acute blood loss and hypovolaemia.
- Trauma and tissue injury, burns.
- Drug reactions, including neuroleptic malignant syndrome (an idiosyncratic complication of antipsychotic drug use, characterized by hyperthermia, rigidity, sweating, and labile blood pressure).
- Intoxication and poisoning, including carbon monoxide poisoning.

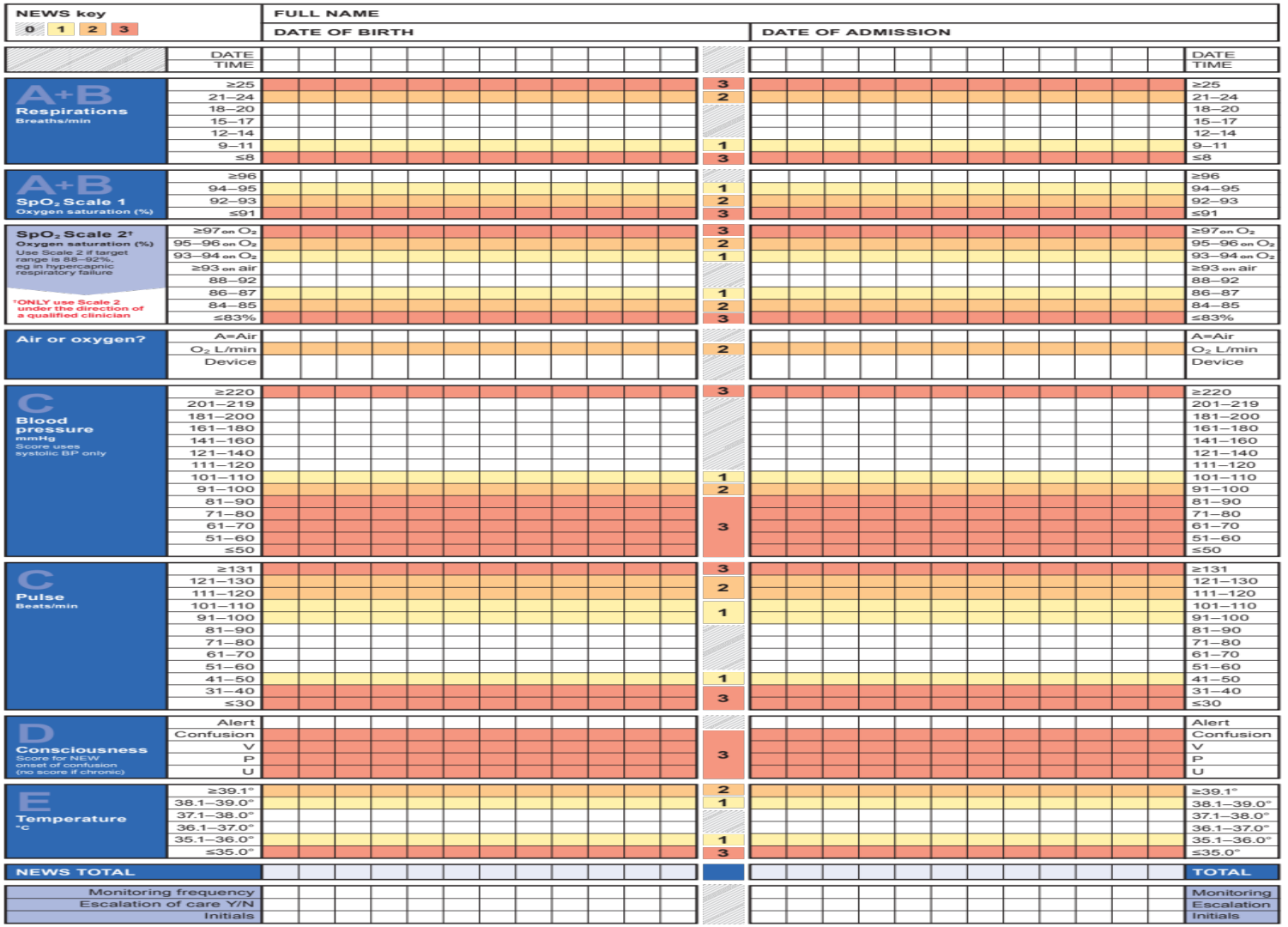
Chart 1: The NEWS scoring system

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

Chart 4: Clinical response to the NEWS trigger thresholds

NEW score	Frequency of monitoring	Clinical response
0	Minimum 12 hourly	• Continue routine NEWS monitoring
Total 1–4	Minimum 4–6 hourly	• Inform registered nurse, who must assess the patient • Registered nurse decides whether increased frequency of monitoring and/or escalation of care is required
3 in single parameter	Minimum 1 hourly	• Registered nurse to inform medical team caring for the patient, who will review and decide whether escalation of care is necessary
Total 5 or more Urgent response threshold	Minimum 1 hourly	• Registered nurse to immediately inform the medical team caring for the patient • Registered nurse to request urgent assessment by a clinician or team with core competencies in the care of acutely ill patients • Provide clinical care in an environment with monitoring facilities
Total 7 or more Emergency response threshold	Continuous monitoring of vital signs	• Registered nurse to immediately inform the medical team caring for the patient – this should be at least at specialist registrar level • Emergency assessment by a team with critical care competencies, including practitioner(s) with advanced airway management skills • Consider transfer of care to a level 2 or 3 clinical care facility, ie higher-dependency unit or ICU • Clinical care in an environment with monitoring facilities

Reproduced from: Royal College of Physicians. *National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS*. Updated report of a working party. London: RCP, 2017.



Reproduced from: Royal College of Physicians. *National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS*. Updated report of a working party. London: RCP, 2017.

Management of Person with suspected sepsis

- **Consider arranging emergency transfer to hospital or ongoing management in primary care, depending on the risk of clinical deterioration from sepsis following assessment and on clinical judgement.**
- If the person has suspected neutropenic sepsis, arrange immediate hospital assessment in secondary or tertiary care..
- If neutropenic sepsis is not suspected, pre-alert secondary care about suspected sepsis and arrange emergency transfer to hospital (usually by 999 ambulance), depending on clinical judgement, if:
  - There are any high risk criteria for severe illness or death from sepsis.
  - A child or young person is aged under 17 years, they are immunocompromised or immunosuppressed, and they have any moderate-to-high risk criteria.
  - There are any moderate-to-high risk criteria *and* the person does not have an identified underlying diagnosis or condition, *and/or* they cannot be safely treated in an out-of-hospital setting.
  - Note: consider managing the person in primary care if they are at high risk of severe illness or death from sepsis, but transfer of care to hospital would be unnecessarily burdensome or inappropriate, for example people who are very frail or approaching the end of life.
  - Note: consider administering broad-spectrum antibiotics if there are any high-risk criteria in a pre-hospital setting, in locations where transfer time is more than one hour, depending on clinical judgement and local protocols.

Risk Criteria

- If there are any moderate-to-high risk criteria for severe illness or death from sepsis *and* a definitive diagnosis or condition has been identified *and* this can be treated in primary care:
  - Manage any underlying condition and arrange further investigations and follow-up as appropriate, depending on clinical judgement.
  - Provide information on symptoms to monitor and clinical features of deterioration, and how to access emergency medical care if needed.
- If there are no high or moderate-to-high risk criteria:
  - Manage the person according to clinical judgement.
  - Provide information on symptoms to monitor and clinical features of deterioration, and how to access emergency medical care if needed.

Complications

Consider assessing for complications following sepsis, if the person is not recovering as expected:If a person has symptoms of anxiety and/or post-traumatic stress disorder,

If a person has persistent fatigue not attributable to other causes, consider referral to occupational therapy and/or physiotherapy for ongoing support. If a person has chronic pain not attributable to other causes, consider referral to a pain clinic for ongoing management.

If a person has recurrent episodes of confirmed sepsis and/or recurrent infections, consider referral to an Immunology specialist to assess for underlying causes of immunocompromise.

If a child has a family history compatible with primary immunodeficiency (such as complement disorders), ensure a referral to a paediatric immunologist has been arranged for further assessment, the urgency depending on clinical judgement

Management in COVID19

- If a person not previously known or suspected to have COVID-19 shows symptoms on presentation, the general advice is to follow UK Government guidance on investigation and initial clinical management of possible cases. This includes information on testing and isolating people.
- During the COVID-19 pandemic, face-to-face examination of people may not be appropriate or possible.
- Therefore, the clinical suspicion of sepsis can be informed by other clinical signs or symptoms, such as:
  - Temperature above 38°C.
  - Respiratory rate above 20 breaths per minute.
  - Heart rate above 100 beats per minute.
  - New confusion.

Assessing Severity

In making an assessment use the following symptoms and signs to help identify people with more severe illness to help make decisions about hospital admission:

- Severe shortness of breath at rest or difficulty breathing.
- Coughing up blood.
- Blue lips or face.
- Feeling cold and clammy with pale or mottled skin.
- Collapse or fainting (syncope).
- New confusion.
- Becoming difficult to rouse.
- Little or no urine output.

Note: in the absence of COVID-19 consider administering antibiotics if the person is critically unwell in a pre-hospital setting in locations where transfer time is more than 1 hour, depending on clinical judgement and local protocols.

SIRS Criteria

- Criteria for SIRS are considered to be met if at least 2 of the following 4 clinical findings are present:
- Temperature higher than 38°C (100.4°F) or lower than 36°C (96.8°F)
- Heart rate (HR) higher than 90 beats/min
- Respiratory rate (RR) higher than 20 breaths/min or arterial carbon dioxide tension ($PaCO_2$) lower than 32 mm Hg
- White blood cell (WBC) count higher than 12,000/µL or lower than 4000/µL or with 10% immature (band) forms

Note that a patient can have a severe infection without meeting SIRS criteria; conversely, SIRS criteria may be present in the setting of many other illnesses not caused by an infectious process (see the image below).

- Healthcare professionals must be alert to the development of sepsis and…
- Educate direct caregivers to report any changes in a patient's condition immediately
- Thoroughly and timely assess patients for suspected infection (risk factors and symptoms) and 2 or more SIRS criteria
- Notify medical provider of findings emergently using SBAR
- Plan to transfer patient to hospital or provide treatment in facility depending on patient/family wishes after reviewing advance directive,
  – Refer for treatment within 3 hours of recognition
- – Consider transferring patient if this timeline cannot be met.

Sepsis Six Bundle in Hospital

- Give oxygen therapy to people with reduced oxygen saturation or with an increase in oxygen requirement over baseline, to maintain oxygen saturation above 94% unless contraindicated.
- Take blood tests and microbiology samples including:
  - Blood gas including glucose and lactate measurement — hypoglycaemia may result from depleted glycogen stores; hyperglycaemia may result from the stress response to sepsis; hyperlactataemia is a non-specific indicator of cellular or metabolic stress and is a marker of illness severity, with a higher level predictive of higher mortality rates.
  - Blood culture — ideally done before antibiotic administration, to identify a primary bacteraemia.
  - Full blood count — white cell count may be high or low; thrombocytopenia may indicate disseminated intravascular coagulation (DIC).
  - C-reactive protein (CRP) — may indicate infection and/or inflammation.
  - Creatinine, urea and electrolytes — may indicate dehydration and/or acute kidney injury.
  - Liver function tests — increased bilirubin or alanine aminotransferase (ALT) levels may indicate cholestasis or other liver dysfunction.
  - Clotting screen — if abnormal may indicate coagulopathy/DIC.
  - Urine analysis and culture, chest X-ray, and additional investigations depending on the person's clinical presentation — this may allow identification of the source of infection, pathogen(s) and sensitivities, and subsequent tailoring and/or de-escalation of antibiotic therapy if appropriate. Source control to eliminate a focus of infection may be possible, such as abscess drainage, debridement of infected tissue, removal of infected devices or foreign bodies, or surgery.

Sepsis Management in Hospital

- Give an intravenous broad-spectrum antibiotic at the maximum recommended dose. The choice of antibiotic will depend on the person's age, clinical presentation, most likely source of infection, recent antibiotic use, and local antibiotic prescribing guidelines.
- Give an intravenous fluid bolus to restore tissue perfusion.
- Check serial lactate measurement.
- Check urine output, monitor fluid balance hourly and monitor the person's clinical condition. This may include using a track-and-trigger scoring system or early warning score to identify people at risk of deterioration

Post Discharge Management

- Provide the person and/or carers with advice on the nature of sepsis, what to expect during recovery after sepsis, and sources of information and support if this has not already been provided in hospital, such as:
  - The UK Sepsis Trust is a national charity (website available at sepsistrust.org) for people or carers affected by sepsis, which has a telephone helpline (telephone 0808 8000029), runs local support groups for survivors of sepsis and their families/carers, and provides patient information booklets The NHS patient leaflet Sepsis.

Education for Families and Patients

- Educate patients and their families about…
- Healthy lifestyle choices such as healthy nutrition and fluid intake
- Need for vaccinations including pneumonia and flu shots
- Always completing full course of antibiotics
- Performing proper hand hygiene frequently
- Chronic disease management and adhering to provider orders
- PREVENTION of infection is PRIMARY!

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