A report for Natural Language Processing

Medical RAG System

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January 9, 2025

Abstract

This project explores the development and enhancement of a Retrieval-Augmented Generation (RAG) system tailored for the domain of medical question answering. The initial implementation utilized datasets such as PubMedQA, Medical Meadow Wikidoc, and MedQA to construct a deduplicated knowledge base, employing sentence embeddings and cosine similarity for context retrieval. While effective in retrieving semantically relevant contexts, the initial system faced challenges in multi-hop reasoning, metadata utilization, and contextual summarization.

To address these limitations, an enhanced RAG system was developed. This system integrates query enrichment with keyword prioritization, leverages metadata (e.g., labels, mesh terms) for targeted filtering, and employs iterative reasoning to combine scattered contexts. A summarization layer using the BART model was added to condense retrieved information into concise, actionable insights. The enhanced system demonstrated improved retrieval precision and contextual relevance, aligning with the needs of medical professionals by synthesizing comprehensive evidence for decision-making. This iterative approach underscores the potential of RAG systems to transform domain-specific applications requiring advanced reasoning and context comprehension.

1 Introduction and Motivation

The rapid advancements in Large Language Models (LLMs) have led to their application across a wide range of use cases. While LLMs excel in tasks such as text summarization and paraphrasing, they often face limitations in other areas, requiring external support to enhance their performance. For instance, domain-specific applications like chatbots may suffer from issues such as providing outdated information or generating hallucinations. A promising solution to these challenges is Retrieval-Augmented Generation (RAG), a hybrid approach that combines information retrieval with text generation to ensure more accurate and contextually relevant outputs.

The necessity for systems that can effectively acquire and synthesize information is highlighted in the medical field by the exponential development of knowledge and the growing complexity of clinical decision-making. It might be difficult for medical practitioners to find accurate, pertinent, and succinct information to help them make judgments. By combining generation models to produce logical, domain-specific outputs and retrieval techniques to extract pertinent information, RAG systems have become a disruptive solution.

The goal of this project is to create a reliable retrieval component for a RAG system that is especially suited to the medical field. In order to provide precise and contextually relevant answers to challenging clinical queries, the system uses three major datasets: MedQA-USMLE, Medical Meadow Wikidoc, and PubMedQA. This prototype places more emphasis on getting information for numerous answer alternatives than standard question-answering systems, enabling medical practitioners to make informed decisions. The core of the RAG system is the retrieval component, which guarantees the precision, applicability, and succinctness of the data supplied.

The urgent need for cutting-edge information tools to assist medical professionals in high-stakes situations where conventional solutions frequently fail serves as the driving force behind this study. By offering focused, evidence-based information that lowers cognitive load and boosts efficiency, this initiative seeks to improve clinical decision-making by addressing the complexity of medical data, including multi-hop thinking and the integration of disparate pieces of evidence. The suggested retrieval component is made to satisfy the particular requirements of the medical field by utilizing developments in natural language processing (NLP), such as semantic similarity retrieval, sentence embeddings, and metadata filtering. Its modular architecture also guarantees scalability and reusability, which makes it easier to integrate into larger RAG systems and expands its use in a variety of medical applications.

This experiment demonstrates how RAG systems have the ability to completely change medical decision support and information retrieval. It seeks to develop a scalable and effective retrieval system that not only satisfies the unique requirements of the medical field but also exhibits versatility for wider applications by utilizing cutting-edge Natural Language Processing (NLP) techniques. Improving the readability and accessibility of complicated medical information is the ultimate goal in order to assist medical practitioners in providing high-quality care.

2 Related Work

Advances in a number of academic areas, including as information retrieval, natural language understanding, and open-domain question answering, have come together to create

Retrieval-Augmented Generation (RAG) systems. The goal of open-domain question answering (OpenQA) systems is to answer queries using large amounts of unstructured data. Conventional OpenQA systems, like DrQA [2], use a two-step process: a reading comprehension model derives answers from appropriate textual sources, and a document retriever finds those sources. Although these systems work well for many tasks, they frequently struggle with multi-hop reasoning, where the solution necessitates combining data from several passages, and with the particular knowledge needed in fields like medicine.

Domain-specific OpenQA systems have gained attention recently, especially in high-stakes industries like healthcare. One prominent example is MEDQA [5], which offers a sizable dataset sourced from professional medical board exams and focuses on intricate clinical questions that require sophisticated reasoning skills and the incorporation of domain-specific information. These datasets highlight how inadequate current methods are at reliably extracting and combining data from various contexts.

The advancement of specialized OpenQA systems has been greatly aided by the availability of high-quality datasets. The PubMedQA [6] dataset, for instance, has biomedical questions that call for models to draw logical conclusions and link symptoms, diagnoses, and therapies. Similar to this, the MedQA-USMLE dataset [5] has multiple-choice questions that mimic actual clinical situations, making it difficult for systems to find evidence and reach well-informed conclusions. These are supplemented by the Medical Meadow Wikidoc collection, which offers a wealth of textual resources that call for combining disparate pieces of evidence into logical answers.

Embedding-based retrieval techniques have become an essential part of RAG systems in order to get beyond the drawbacks of conventional term-based retrieval systems. Sentence transformers, like *all-MiniLM-L6-v2* [9], create dense embeddings that capture the meaning of text, allowing for more precise semantic similarity retrieval. In the medical field, where precise matches between queries and information sources are uncommon and retrieval algorithms need to take phrasing and language changes into account, this development is especially beneficial.

Despite these developments, there are still a number of obstacles to overcome when using NLP to answer medical questions. Retrieval failures and incomplete reasoning chains are frequently caused by the intricacy of medical terminology, the requirement for multi-hop reasoning, and the dependence on domain-specific terminology. Previous studies, notably MEDIQA [1], have emphasized these drawbacks and suggested ways to improve system performance, such as metadata integration, iterative retrieval techniques, and keyword prioritizing.

Building on those results, this project takes advantage of the advantages of metadata utilization and embedding-based retrieval to meet the particular requirements of medical question answering. The system seeks to develop RAG designs in managing intricate, domain-specific activities by integrating cutting-edge methods including multi-hop reasoning, keyword prioritizing, and a summarization layer. Through these contributions, this study lays the groundwork for implementing RAG systems in additional specialized disciplines in addition to addressing the difficulties associated with information retrieval in the medical field.

3 Data Materials and Analysis

This study leverages three datasets to construct a Retrieval-Augmented Generation (RAG) system for medical question-answering tasks. The first dataset, **MedQA-USMLE-4-options** [3], provides multiple-choice medical questions with features such as questions, options, correct answers, and metamap_phrases. For this RAG system, the "question" and "options" were used as queries to retrieve relevant information. The second dataset, **medical meadow wikidoc** [7], includes question-answer pairs with context provided in the "output" column, which was incorporated into the knowledge base for retrieval. The third dataset, **PubMedQA** [8], comprises three subsets: labeled, unlabeled, and artificial, with contexts organized as dictionaries including "contexts," "labels," and "meshes." For the RAG system, the "context" column was used, while "labels" and "meshes" served as metadata to enhance retrieval relevance.

3.1 Analysis

An analysis of the datasets revealed significant thematic alignment between Dataset 1's question-options pairs and the contexts provided in Datasets 2 and 3. Common terms such as "patient," "symptoms," and "treatment" appeared across all datasets, indicating shared medical themes. In Dataset 2, the "output" column contained relevant clinical knowledge that aligns with Dataset 1's diagnostic and management questions. For instance, frequent terms like "syndrome," "disease," and "treatment" in Dataset 2's word cloud highlight its suitability for providing medical evidence to answer Dataset 1's queries.

A detailed keyword analysis of Dataset 1's "options" revealed a total of **15,149 unique keywords**, highlighting its diverse vocabulary. When comparing these keywords against the knowledge datasets, **3,234 keywords were not found in Dataset 2** and **923 keywords were missing in artificial dataset**. This indicates strong, but not complete, overlap with the knowledge datasets, suggesting areas for potential improvement in coverage and alignment.

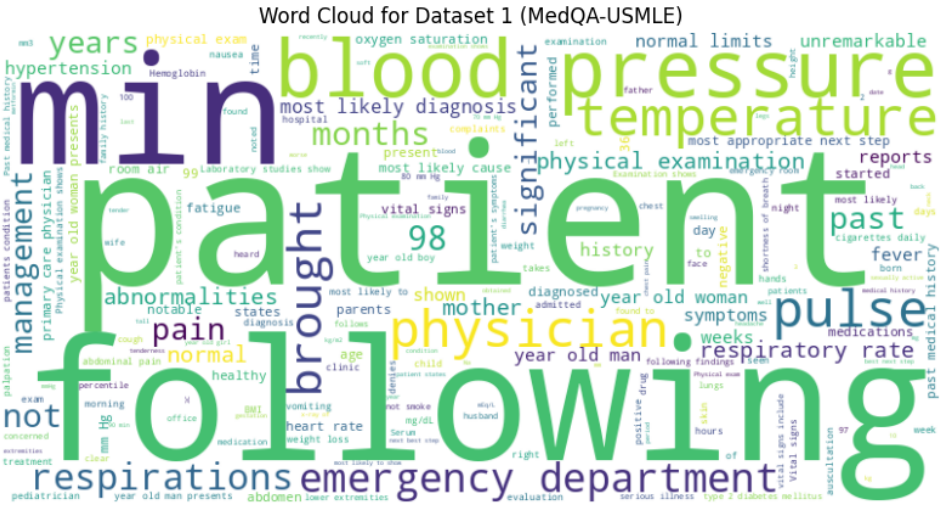

Figure 1: Word Cloud for Dataset 1 (GBaker/MedQA-USMLE-4-options)

Dataset 3 further complements Dataset 1 with research-focused contexts. The artificial subset of Dataset 3 showed significant overlap with Dataset 1, containing terms such

as "patient," "study," and "significant," which align with Dataset 1's focus on clinical reasoning. Similarly, the labeled and unlabeled subsets included contextual information enriched with metadata ("labels" and "meshes"), which enhances retrieval relevance by providing structured domain-specific knowledge.

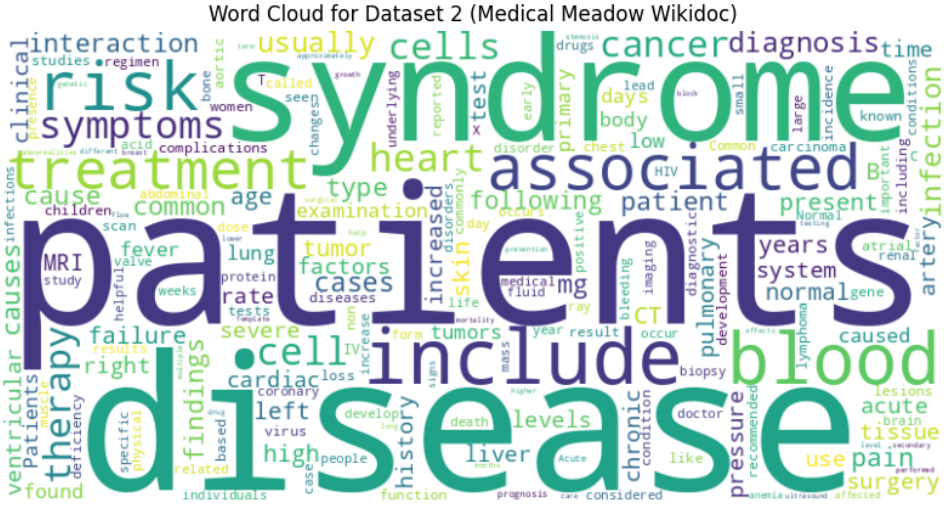

Figure 2: Word Cloud for Dataset 2 (medalpaca/medical_meadow_wikidoc)

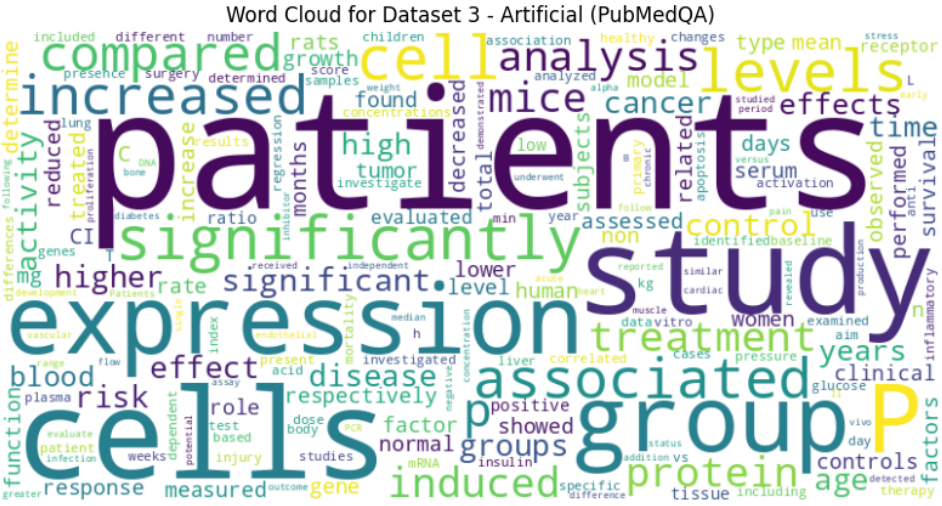

Figure 3: Word Cloud for Dataset 3 (qiaojin/PubMedQA - Artificial, Labeled, and Unlabeled)

Despite these challenges, the question-options pairs from Dataset 1 are well-represented in Datasets 2 and 3, particularly in areas related to patient cases, diagnostic reasoning, and treatment strategies. This alignment underscores the potential of using these datasets collectively to develop an effective RAG system capable of retrieving and presenting clinically relevant information to support medical decision-making.

4 Methodology

The Retrieval-Augmented Generation (RAG) system has been developed iteratively, beginning with a basic implementation and moving to a more robust, advanced version to fulfill the specific needs of medical question answering. This section gives an overview of the initial implementation and a full description of the advanced system.

The initial implementation used the MiniLM-L6-v2 model to generate embeddings for contexts and queries, which was chosen for its balance of computational efficiency and semantic accuracy. The algorithm used cosine similarity to rank contexts based on their relevance to the question and returned the top-k results. Although functional, this technique had shortcomings in handling huge texts and prioritizing crucial terms. To address these inadequacies, we developed a more advanced system with significant improvements.

To overcome constraints, the improved RAG system provided major improvements. First, chunking was used to better manage huge texts. A new class was used to partition texts into fixed-length overlapping chunks, inspired by Mehul Jethva's RAG chunking work [4]. This preserved semantic continuity and enabled finer-grained retrieval. Metadata associated with each chunk, such as labels and mesh words, were used to filter and rank results.

Keyword prioritizing helped to improve the retrieval process. Keywords from queries and answer options were used in the embedding generation process. These were integrated with primary text embeddings and weighted to emphasize essential phrases, resulting in more relevant context retrieval. FAISS (Facebook AI Similarity Search) was incorporated to efficiently manage the high volume of embeddings. FAISS indexes embeddings and uses quick similarity-based retrieval to reduce query times while retaining high precision.

An additional improvement is the application of metadata for context ranking. In order to filter and rank the retrieved contexts, metadata like labels and mesh terms were used, resulting in more precise and domain-specific outcomes.

To provide outputs that are clear and easy to understand, a summary layer was added at the end. By giving users actionable insights, the `bart-base` model was able to summarize the retrieved contexts and lessen their cognitive load. A scalable, accurate, and user-friendly RAG system was produced by combining effective retrieval, information use, and summarizing techniques.

The workflow for the advanced system is as follows:

1. Preprocess the data by chunking texts and associating metadata such as labels and mesh terms.

2. Generate embeddings for text chunks and queries using the `all-MiniLM-L6-v2` model.

3. Index embeddings with FAISS for efficient similarity-based retrieval.

4. Retrieve top-k contexts for each query, prioritizing keywords and filtering with metadata.

5. Summarize the retrieved contexts using `bart-base` to generate concise outputs.

These advancements addressed the limitations of the initial system, creating a robust pipeline capable of handling the complexities of medical question answering efficiently.

5 Experiments

The Retrieval-Augmented Generation (RAG) system has been created and evaluated through many iterations, beginning with an early implementation and gradually improving the methodology to solve noted constraints. The `all-MiniLM-L6-v2` model was utilized for embedding creation in the original system because of its computational efficiency and lightweight design. The relevance between query and context embeddings was measured using cosine similarity, which allowed the top k relevant contexts for each query to be retrieved. Although this baseline system showed basic capabilities, it struggled to handle sophisticated queries, especially ones that required multi-hop reasoning or domain-specific phrase prioritization. Retrieval and relevance matching were also inefficient due to the system's lack of tools for efficiently processing huge texts.

Additionally, I attempt to develop a hybrid retrieval system in this experiment that combines dense embedding-based approaches for document retrieval and rating with BM25. To improve the query representation, the dense retrieval component used a weighted embedding fusion technique. In particular, the query context embedding (50%), question embedding (30%), and option embedding (20%) were weighted to create the final query embedding. Normalization was performed after this weighted fusion to guarantee a consistent scale for calculating similarity. The retrieval system then balanced the contributions of lexical and semantic similarity by fusing the outcomes of dense retrieval and BM25 using a weighted scoring mechanism. This hybrid technique, however, was inappropriate for the system's needs and failed to produce appreciable performance advantages.

Finally, the new system was created with an emphasis on cutting-edge methods in recognition of these difficulties. Chunking was developed to allow for finer-grained retrieval while maintaining semantic continuity by breaking up huge texts into digestible chunks of 300 tokens with a 50-token overlap. By combining keyword embeddings with main text embeddings and giving keywords higher weights, keyword prioritizing was used to highlight important terms inside queries and contexts, increasing relevancy. The system was able to filter and rank contexts according to domain-specific properties by using metadata like labels and MeSH phrases to refine retrieval. The FAISS (Facebook AI Similarity Search) library was incorporated to index embeddings and carry out similarity-based retrieval in order to increase efficiency. In comparison to conventional brute-force techniques, this greatly shortened the retrieval time. To generate embeddings, the RoBERTa model was also tested, but it was found to be less effective and more resource-intensive than `all-MiniLM-L6-v2`. Although RoBERTa demonstrated more theoretical accuracy, in this case, its computing cost was greater than its advantages. `all-MiniLM-L6-v2` was therefore kept since it strikes a balance between accuracy and speed. Together, these improvements addressed the shortcomings of previous implementations while presenting up the possibility for reliable and scalable performance by creating a system that can effectively retrieve and summarize pertinent contexts for medical question answering.

6 Results and Discussion

In this section, we present a detailed analysis of the performance of the initial and advanced RAG (Retrieval-Augmented Generation) systems. The evaluation focuses on scenarios where the initial RAG system performs well and retrieves relevant and mean-

ingful contexts, as well as cases where it falls short in providing actionable or clinically appropriate information. For each identified limitation, we discuss how the advanced RAG system addresses these gaps by leveraging improved retrieval strategies, context relevance, and summarization capabilities.

In the example presented in Appendix A.2, the initial RAG system performs well in retrieving relevant context for the given options, particularly for **Option A: Placing the infant in a supine position on a firm mattress while sleeping**. The retrieved context highlights evidence supporting the recommendation for supine sleeping, citing increased adherence to the American Academy of Pediatrics guidelines after educational interventions. This directly aligns with the precautionary measures to reduce the risk of sudden infant death syndrome (SIDS), making the context both meaningful and actionable. By focusing on behavioral changes and evidence-based recommendations, the initial RAG system provides a clear and clinically relevant explanation, demonstrating its effectiveness for this scenario. However, the initial RAG system shows limitations in other cases. As illustrated in the example from Appendix A.5, the system fails to retrieve relevant and actionable contexts for diagnosing the likely cause of a 20-year-old woman's menorrhagia, bruising, and family history of similar symptoms. For **Option A: Hemophilia A**, the retrieved context provides a broad historical overview of the condition, lacking any focus on the clinical presentation or relevance to the patient's case. Similarly, for **Option B: Lupus Anticoagulant** and **Option C: Protein C Deficiency**, the system retrieves tangential information centered on technical testing protocols and genetic details, without addressing the patient's symptoms or laboratory findings. Although the context for **Option D: Von Willebrand Disease** includes diagnostic elements like tests and expected results, it fails to directly relate to the clinical presentation or emphasize that Von Willebrand Disease is a common hereditary bleeding disorder, which strongly aligns with the patient's case. Overall, while the initial RAG system demonstrates strengths in certain scenarios, such as retrieving actionable content for SIDS prevention, it prioritizes general or academic information in other cases, limiting its ability to address focused diagnostic scenarios effectively.

The advanced RAG system addresses the limitations of the initial system by incorporating techniques such as efficient text chunking, FAISS-based vector similarity search, keyword-prioritized query embeddings, and BART-based summarization. These enhancements improve the relevance, specificity, and clarity of the retrieved information, making the system more effective in providing actionable and contextually appropriate content. As mentioned in Appendix A.3, the advanced RAG system demonstrates significant improvements over the initial RAG system in retrieving relevant and actionable contexts. The advanced system effectively addresses the limitations of the initial system by focusing on the embryologic basis of the condition and providing clinically meaningful information. The comparison of both systems is outlined in the table below:

Table 1: Comparison of the Initial and Advanced RAG Systems

Option	**Context(Initial RAG)**	**Context(Advanced RAG)**	**Analysis**
A:Abnormal migration of ventral pancreatic bud	Discusses pancreatic transplantation and progenitor cells but lacks relevance to embryologic errors or clinical symptoms.	Provides embryologic details about pancreatic development, linking digestive problems in infants to underdeveloped pancreatic function.	The advanced system provides a focused and relevant embryologic explanation, while the initial system fails to connect its context to the clinical scenario.
B:Complete failure of proximal duodenum to recanalize	Discusses technical aspects of duodenal resection and manometry, unrelated to embryologic development or symptoms.	Refers to meconium peritonitis and related complications like vomiting and bowel dilation, connecting embryologic bowel issues to symptoms.	The advanced system ties embryologic abnormalities to clinical presentation, while the initial system's context is unrelated.
C:Abnormal hypertrophy of the pylorus	General description of hypertrophic pyloric stenosis with irrelevant hypotheses like pesticide exposure and unrelated surgical procedures.	Focuses on the incidence and characteristics of bilious vomiting in infants with hypertrophic pyloric stenosis, aligning with the infant's symptoms.	The advanced system delivers clinically relevant context, emphasizing characteristic symptoms, while the initial system includes unrelated information.
D:Failure of lateral body folds to move ventrally and fuse in the midline	Discusses spinal ligament deformations, unrelated to embryologic development or abdominal issues.	Mentions fetal deficiencies like umbilical hernias that could potentially be linked to the symptoms.	The advanced system provides embryologic context with potential links to the clinical presentation, while the initial system completely fails to address the question.

The comparison clearly demonstrates that in many cases, the advanced RAG system generates significantly better and more relevant contexts compared to the initial RAG system. These improved contexts provide greater clarity and actionable insights, allowing medical professionals to make informed decisions and determine the most appropriate answers based on the retrieved information. However, there are still areas where the advanced RAG system can be further improved to enhance its utility in medical decision-making.

Discussion To address the remaining limitations, future work can focus on fine-tuning the RAG system using domain-specific datasets to better capture medical nuances and improve retrieval accuracy. Replacing the current model with domain-specific pretrained models such as BioBERT, ClinicalBERT, or RoBERTa could enhance the system's understanding of medical terminology and improve contextual relevance. Additionally, incorporating advanced techniques like context-aware embeddings, dynamic query reformulation, and reinforcement learning can refine the system's ability to prioritize clinically significant details. Expanding the knowledge base with curated, high-quality medical literature and leveraging hybrid retrieval models that combine symbolic and neural approaches could further improve the system's performance in underrepresented areas. These advancements will ensure that the RAG system becomes a more reliable and robust tool

for aiding medical professionals in decision-making.

7 Conclusion

Overall, by addressing the shortcomings of the initial implementation and expanding the system's capabilities, this study showed how to construct a Retrieval-Augmented Generation (RAG) system specifically designed for medical question answering. Basic retrieval capabilities was offered by the Initial RAG system, but it needed improvement due to issues with multi-hop reasoning, term prioritization, and semantic comprehension. Complex medical queries were successfully supported by the Advanced RAG system, which successfully combined chunking, metadata use, and sophisticated retrieval processes to increase precision and contextual relevance. The technology gave consumers actionable insights with less cognitive strain by utilizing enhanced query processing and summarizing techniques. Future developments, such as fine-tuning on models like BioBERT and RoBERTa and utilizing sophisticated similarity and query optimization techniques, offer significant advances even though addressing unusual or highly specialized cases still presents hurdles. The potential of RAG systems to transform domain-specific decision support, especially in vital domains like medicine, is shown by this work.

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Appendix

A Detailed Contexts for Initial and Advanced RAG System

A.1 Question

Question: A 23-year-old pregnant woman at 22 weeks gestation presents with burning upon urination. She states it started 1 day ago and has been worsening despite drinking more water and taking cranberry extract. She otherwise feels well and is followed by a doctor for her pregnancy. Her temperature is 97.7°F (36.5°C), blood pressure is 122/77 mmHg, pulse is 80/min, respirations are 19/min, and oxygen saturation is 98% on room air. Physical exam is notable for an absence of costovertebral angle tenderness and a gravid uterus. Which of the following is the best treatment for this patient?

Option A: Ampicillin
Context of the initial RAG: We selected patients with histories of immediate reactions to penicillins and positive results to skin tests for one or more penicillin reagents (PPL, MDM, or benzylpenicillin), one or more semi-synthetic penicillins (ampicillin, amoxicillin, or piperacillin), or both. Take ampicillin at least 1 hour before or 2 hours after meals. Standard treatment (mostly semisynthetic penicillin) (n = 190) or that combined with levofloxacin (n = 191). Supplementary rifampicin was recommended if deep infection was suspected....

Context of the Advance RAG: chances of urinary tract infections (UTI) have been reported. Urinary tract infections(UTi) in prenatal babies raise the suspicion of underlying renal abnormality. So in these patients antibiotic prophylaxis is started as soon as possible after the delivery until exclude the diagnosis with either VUR or obstructive uropathy.Urinary stone incidence in pregnancy has been reported in a wide range, from 1 in 200 to 1 in 2000 cases.

Option B: Ceftriaxone
Context of the initial RAG: Peak serum ceftriaxone concentrations were well above the minimal inhibitory concentration for 90% of strains. Trough serum concentrations of the drug prior to the next dose were also considerably in excess of the minimal inhibitory concentration. In the prevention group, 8 of 65 developed an infection, which was sensitive to ceftriaxone, whereas in 22 of the 39 patients from the treatment group, cultures showed organisms sensitive to ceftriaxone and in the remaining 17 patients sensitivity was not done. Although the neuroprotective effect of ceftriaxone (CTX) has been reported, the underlying mechanisms are still uncertain. In this study, we investigated if rats recover better from CTX pret...

Context of the Advance RAG: Increased ESR and CRP Ultrasound Sudden onset sever pain with nausea and vomiting Pregnancy Ruptured ectopic pregnancy - RLQ / LLQ - - - N Positive pregnancy test Ultrasounded History of missed period and vaginal bleeding Functional Irritable Bowel Syndrome - Diffuse - - / - N Clinical diagnosis ROME III/IV criteria Pharmacologic studies based criteria - High dietary fiber Osmotic laxatives Antispasmodic drugs References ↑ Burns, Cart

Option C: Doxycycline
Context of the initial RAG: Doxycycline has a high degree of activity against many common respiratory pathogens and has been used in the outpatient management of lower respiratory tract infections, including pneumonia. To understand the differential responses to doxycycline between Caucasian and Hispanic patients observed in a previous clinical trial. After treatment with doxycycline 71% of the women were symptom-free or had a subjective decrease in symptoms....

Context of the Advance RAG: testing may be helpful in identifying women at risk for acute allergic reactions. Tetracycline and doxycycline usually are not used during pregnancy. Erythromycin and azithromycin should not be used, because neither reliably cures maternal infection or treats an infected fetus. Data are insufficient to recommend ceftriaxone for treatment of maternal infection and prevention of congenital syphilis. Placental inflammation from congenital infection might increase the risk for perinatal

Option D: Nitrofurantoin
Context of the initial RAG: Nitrofurantoin is a nitroderivative antibiotic that has bactericidal activity against pathogens causing urinary tract infection. A few studies have reported that nitrofurantoin has cytotoxic activity against cancer cells; however, nitrofurans remain a poorly explored class of compounds with respect to their anticancer potential. The aim of this study was to investigate the anticancer effects of a nitrofurantoin derivative, n-pentyl-nitrofurantoin (NFP), on HL-60 leukemia cells. Nitrofurantoin pharmacokinetics were studied in an open-label, single-oral dose (100 mg) study in 36 male Chinese subjects who were pre-screened for ABCG2 421 CC, CA and AA genotypes (n = 12 each). Plasma and urine co...

Context of the Advance RAG: Our objective was to determine if maternal urinary cyclic guanosine monophosphate levels are altered in preeclampsia and preeclamptic pregnant women. Aliquots from 24-hour urine samples collected from 57 women with preeclampia and 14 normotensive pregnant women in the third trimester of pregnancy were assayed. Urinary cyclic Guanosine Monophosphates values were expressed per milligram of urinary creatinine to standardize for renal

A.2 Question

Question: A 3-month-old baby died suddenly at night while asleep. His mother noticed that he had died only after she awoke in the morning. No cause of death was determined based on the autopsy. Which of the following precautions could have prevented the death of the baby?

Option A: Placing the infant in a supine position on a firm mattress while sleeping
Context of the initial RAG: To determine whether premature infants' sleep organization, total sleep time, and arousals may be modulated while on a conformational positioner that provides boundaries, customized positioning, and containment compared with standard positioning (standard crib mattress). A total of 96 child care providers attended the educational in-service. Providers who were using the supine position exclu-

sively increased from 44.8% to 78.1%. This change in behavior was sustained, with 85% of centers placing infants exclusively supine 6 months after the intervention. Awareness of the American Academy of Pediatrics recommendation of supine as the preferred position for infants increased from 47.9% to 78.1%,...

Context of the Advance RAG: infant sleep, applied as a population strategy of prevention from the first weeks and months, risk unintended outcomes, including increased amounts of problem crying, premature cessation of breastfeeding, worsened maternal anxiety, and, if the infant is required to sleep either day or night in a room separate from the caregiver, an increased risk of SIDS. In current literature the prognosis of trisomy 18 is mainly described as inevitably lethal. After intervention of parental intervention in the first week of life,

Option B: Keeping the infant covered and maintaining a high room temperature
Context of the initial RAG:: Newborn infants, in particular those needing resuscitation maneuvers at birth, must be readily positioned under a radiant infant warmer (RIW). However, temperature of exposure and/or level of RIW power to set up are not specified. We aimed to evaluate the temperature of exposure generated by three different RIWs at pre-selected power outputs and to assess whether the delivery room temperature may affect this condition. To improve admission temperatures of preterm infants ¡ or =31 weeks gestation by increasing the ambient temperature in the operating theatre and wrapping in polyethylene wrap at caesarean section. To evaluate the influence of ambient temperature on infants' arousability from s...

Context of the Advance RAG: To examine the long-term effects of neonatal hypothermia (HT) on survival. Using the longitudinal community and hospital surveillance system of the Bandim Health Project, we followed children born between 1997 and 2002 at the only maternity ward in the city. All children's axillary temperature was measured within 12 h of birth. They were followed from birth to 6 months of life through regular home visits. We identified 2926 live births in the study area and 177 deaths before 6 months.

Option C: Application of a device to maintain the sleeping position
Context of the initial RAG: University-affiliated sleep laboratory. Research and sleep laboratories. Two university-affiliated sleep laboratories....

Context of the Advance RAG: SIDS mortality is higher during the night than in the day. (1) To examine risk factors for SIDS by time of day and (2) to see if the proportion of deaths at night has changed from prior to the 'Back to Sleep' campaign, which recommended infants sleep supine. A large population-based SIDS matched case-control (GeSID) study conducted from 1998 to 2001 (when the prevalence of infants placed prone to sleep was 4.1%).

Option D: Avoiding pacifier use during sleep
Context of the initial RAG: It has been reported that pacifiers might reduce the risk of SIDS by favouring infants' arousability from sleep. We evaluated the influence of a pacifier on the frequency and duration of spontaneous arousals in healthy infants. Polygraphic recordings were performed in 14 infants with an age of 51.7+/-19.9 days (means+/-

SD) who regularly used a pacifier during sleep. Cortical and subcortical arousals were scored according to the recommendations of the "International Paediatric Work Group on Arousals." The number of arousals per 10-min-period and the duration of arousals were determined for periods of pacifier use as well as for periods after pacifier dislodgement and were compared with the da...

Context of the Advance RAG: Impaired arousal from sleep has been implicated in sudden infant death syndrome (SIDS). Sleeping in the prone position is a major risk factor for SIDS. Epidemiological studies have shown that pacifier use decreases the risk of SIDS, even when infants sleep prone. We examined spontaneous arousability in infants slept prone and supine over the first 6 months of life and hypothesised that spontaneous arousals would be increased in pacifier users. Healthy term infants (n = 30) were studied

A.3 Question

Question: A mother brings her 3-week-old infant to the pediatrician's office because she is concerned about his feeding habits. He was born without complications and has not had any medical problems up until this time. However, for the past 4 days, he has been fussy, is regurgitating all of his feeds, and his vomit is yellow in color. On physical exam, the child's abdomen is minimally distended but no other abnormalities are appreciated. Which of the following embryologic errors could account for this presentation?

Option A: Abnormal migration of ventral pancreatic bud
Context of the initial RAG: The transplanted pancreatic bud rapidly engrafts and vascularises when transplanted into the ACE. The pancreatic progenitor cells differentiate into exocrine and endocrine cells, including cells expressing insulin, glucagon and somatostatin. The morphology of the transplanted pancreatic bud resembles that of the native developing pancreas. Beta cells within the transplanted pancreatic bud respond to glucose in a manner similar to that of native fetal beta cells and superior to that of in vitro developed beta cells. Unlike in vitro grown pancreatic explants, pancreatic tissue developing in the ACE is vascularised, providing the developing pancreatic tissue with a milieu resembling the native ...

Context of the Advance RAG: The pancreas forms from the endoderm, which is responsible for the production of the tissue within the pancreatreas, lungs, and thyroids. The Pancreas starts to form in the tenth week in fetal development. In the twelfth week the islets of Langerhan start to show. The pancreaas is fully matured by the age of two. Therefore, infants show digestive problems due to the fact that their pancreases is unable to secrete

Option B: Complete failure of proximal duodenum to recanalize
Context of the initial RAG: In controls, a cannula was inserted into the duodenum opposite the papilla for retrograde manometry. In the duodenectomy group, the entire duodenum was resected, while preserving the papilla, which was implanted into the jejunum, and the cannula was placed. Sphincter motility was recorded after bolus injections

of 20 and 100 ng/kg of CCK-OP. A retrospective review of 22 patients who underwent surgery for suspected GIST involving the duodenum. We verified whether analyzing both rearrangements in duodenal biopsies from RCD patients increases the diagnostic accuracy of this method....

Context of the Advance RAG: peritonitis Meconium peritonitis refers to rupture of the bowel prior to birth, resulting in fetal stool (meconia) escaping into the surrounding space (peritoneum) leading to inflammation (peritonis). Despite the bowel rupture, many infants born after meconium perionitis in utero have normal bowels and have no further issues. Twenty percent of infants born with meconia peritonis will have vomiting and dilated bowels on

Option C: Abnormal hypertrophy of the pylorus
Context of the initial RAG: Hypertrophic pyloric stenosis (HPS) is a condition noted within the first several weeks of life that results in hypertrophy of the pyloric muscle between the stomach and duodenum. The etiology has not been elucidated but genetic and environmental influences are suspected. We hypothesized that agricultural pesticides would be associated with an increased incidence of pyloric stenosis. The pylorus-preserving technique has been performed on two patients suffering from severe hypercholesterolaemia and hyperglycaemia and who were not more than 30% overweight, at Clinica Chirurgica and Chirurgia d'Urgenza Department, University of Sassari, Italy. Both patients had a six-month follow-up assessment....

Context of the Advance RAG: To describe the incidence of bilious vomiting in infants with infantile hypertrophic pyloric stenosis that presented to a pediatric emergency department. A retrospective medical record review included all infants who presented to our level 1 pediatric emergency emergency department from January 1, 2005, through December 31, 2009, who were diagnosed intraoperatively with infants. Emesis was determined to be bilious if the vomit was described as "green," "containing bile," or "bilious." The authors identified

Option D: Failure of lateral body folds to move ventrally and fuse in the midline
Context of the initial RAG: Inhomogeneous in-plane and through-plane shear deformations were prominent through the middle body of the FCL on both surfaces. Anterior surface deformations were more pronounced because of the small width of the joint space, whereas posterior surface deformations were more diffuse because the larger area increased deformability. We speculate these areas of large deformation may provide this proprioceptive system with an excellent measure of spinal motion. This deformity arises with minimal trauma and is difficult to reproduce in cadaveric spines. We hypothesize that wedging is created by a 2-stage process. First, excessive loading damages a vertebral endplate and decompresses the adjacent i...

Context of the Advance RAG: If fetal deficiency was severe because of complete absence (athyreosis) of the gland, physical features may include a larger anterior fontanel, persistence of a posterior fontanal, an umbilical hernia, and a large tongue (macroglossia). Without therapy, the child later may show signs of neurological impairment. We sought to determine the relationship between the degree of stomach herniation by antenatal sonography and neonatal outcomes in fetuses with isolated left-

A.4 Question

Question: A pulmonary autopsy specimen from a 58-year-old woman who died of acute hypoxic respiratory failure was examined. She had recently undergone surgery for a fractured femur 3 months ago. Initial hospital course was uncomplicated, and she was discharged to a rehab facility in good health. Shortly after discharge home from rehab, she developed sudden shortness of breath and had cardiac arrest. Resuscitation was unsuccessful. On histological examination of lung tissue, fibrous connective tissue around the lumen of the pulmonary artery is observed. Which of the following is the most likely pathogenesis for the present findings?

Option A: Thromboembolism
Context of the initial RAG: Thromboembolism is a general term describing both thrombosis and its main complication which is embolism. The history of venous thromboembolism (VTE), and the rationale for thromboprophylaxis in surgical patients are well understood. The situation is less clear for acutely ill medical patients. Venous thromboembolism is a common source of morbidity and mortality but a variety of preventative measures are available....

Context of the Advance RAG: conditions that affect the pulmonary circulation. Examples of these conditions are: Pulmonary embolism, a blood clot that forms in a vein, breaks free, travels through the heart and lodges in the lungs (thromboembolism). Large pulmonary emboli are fatal, causing sudden death. A number of other substances can also embolise to the lungs but they are much more rare: fat embolisms (particularly after bony injury), amniotic fluid emb

Option B: Pulmonary ischemia
Context of the initial RAG: Pulmonary ischemia-reperfusion is a pathological process seen in several clinical conditions, including lung transplantation, cardiopulmonary bypass, resuscitation for circulatory arrest, atherosclerosis, and pulmonary embolism. A better understanding of its molecular mechanisms is very important. Ischemic preconditioning achieved by brief periods of ischemia followed by reperfusion before a prolonged period of ischemia, is well known to reduce myocardial damage. We investigated whether ischemic preconditioning of the lung could also attenuate ischemia-reperfusion injury following pulmonary preservation. Acute lung injury is a recognized complication of lower limb ischemia-reperfusion that h...

Context of the Advance RAG: Ischemic preconditioning achieved by brief periods of ischemia followed by reperfusion before a prolonged period of amchemia, is well known to reduce myocardial damage. We investigated whether ischemic preconditionsing of the lung could also attenuate ischemia-reperfusion injury following pulmonary preservation. Transient ischemias of the right lung was achieved in rabbits (n = 4 in each group) by occluding the main

Option C: Pulmonary hypertension
Context of the initial RAG: Pulmonary hypertension is defined by a mean pulmonary arterial pressure higher than 25mmHg. It can be assessed by echocardiography, the diagnostic study of choice due to its low risk and useful information that it can provide, and right heart cardiac catheterization to confirm the diagnosis. Pulmonary hypertension is a common complication of chronic hypoxic lung diseases and is associated with increased morbidity and reduced survival. The pulmonary vascular changes in response to hypoxia, both structural and functional, are unique to this circulation. Twenty-seven patients with pulmonary hypertension: 7 with primary, and 20 with secondary pulmonary hypertension of various causes. The control...

Context of the Advance RAG: of pulmonary arteries. during hypoxia-induced pulmonary hypertension. Pulmonary hypertension (PH) is associated with increased mortality in fibrotic idiopathic interstitial pneumonia (IIP). We hypothesize that baseline K(CO) (diffusing capacity of carbon monoxide/alveolar volume) and 6-month decline in K(C) reflect PH, thus predicting mortality in IIP. All IIP referrals (2004-2007) were identified (n = 269

Option D: Pulmonary passive congestion
Context of the initial RAG: The prevalence of pulmonary congestion in the setting of CS is uncertain. We tested the hypothesis that passive congestion is more important than poor perfusion. To establish reference values, describe reproducibility, and investigate the diagnostic and monitoring properties in relation to pulmonary congestion of new pulmonary gas exchange parameters describing ventilation/perfusion mismatch (variable fraction of ventilation [fA2] or the drop in oxygen pressure from the mixed alveolar air of the two ventilated compartments to the nonshunted end-capillary blood [DeltaPO(2)]) and pulmonary shunt....

Context of the Advance RAG: Chronic obstructive pulmonary disease can be diagnostically evaluated by physical examination through auscultation. Physical examination are quite specific and sensitive for severe disease. The signs are usually difficult to detect in cases of mild to moderate diseases. Findings on general physical examination can be cyanosis, tachypnea, use of accessory respiratory muscles, paradoxical indrawing of lower intercostal spaces is evident (known as the Hoover sign), elevated jugular venous pulse and peripheral

A.5 Question

Question: A 20-year-old woman presents with menorrhagia for the past several years. She says that her menses "have always been heavy", and she has experienced easy bruising for as long as she can remember. Family history is significant for her mother, who had similar problems with bruising easily. The patient's vital signs include: heart rate 98/min, respiratory rate 14/min, temperature 36.1°C (96.9°F), and blood pressure 110/87 mm Hg. Physical examination is unremarkable. Laboratory tests show the following: platelet count 200,000/mm3, PT 12 seconds, and PTT 43 seconds. Which of the following is the most likely cause of this patient's symptoms?

Option A: Hemophilia A
Context of the initial RAG: Hemophilia is considered a very old disease with its history dating back to the 2nd century AD. The first modern descriptions of the condition appeared during the 19th century. Extensive work has been done over the centuries regarding the classification, inheritance pattern, and treatment of hemophilia. Haemophilia B (HB) was described in 1952 as a single disease for the first time. In comparison to haemophilia A (HA) the bleeding tendency seemed to be less severe. The aim of this study was to investigate this hypothesis in all patients with HA and HB treated in the haemophilia care center of the Vivantes Klinikum. Hemophilia A (HA) is a congenital bleeding disorder resulting from factor VII...

Context of the Advance RAG: Symptoms of thrombocytopenia, or a lowered platelet count, leads to bruising and potentially life-threatening haemorrhage. The history of HIT always involves exposure to heparin. Typical features of a patient's history depend on the type and location of thromabosis and whether the platelet counts is sufficiently low to result in bleeding. Venous and arterial thrombinoses can result in variable symptoms. Symptoms of deep vein throm

Option B: Lupus anticoagulant
Context of the initial RAG: To investigate whether a single positive test for lupus anticoagulant (LA) is associated with levels of inflammatory markers and traditional cardiovascular risk factors, independent of autoimmune disease, thrombophilia and occurrence of other antiphospholipid antibodies. Recent guidelines for lupus anticoagulant (LA) detection recommend mixing test interpretation with either a mixing test-specific cut-off (MTC) or index of circulating anticoagulant (ICA). Few studies directly compare efficacy of these approaches. We retrospectively applied MTC and ICA assessment to raw data of 350 LA-positive plasmas from non-anticoagulated patients to compare detection rates of inhibition. To assess the per...

Context of the Advance RAG: Antiphospholipid antibodies, both anticardiolipin and lupus anticoagulant, are common in SLE. We asked, in a prospective cohort, whether these antibodies are predictive of atherosclerosis and/or coronary artery disease. Three hundred eighty patients, 92% female, 49% Caucasian, 51% African-American, mean age 46.4+/-12.3 years are followed quarterly, with assessment of both antiardiolisin

Option C: Protein C deficiency
Context of the initial RAG: Protein C deficiency is a genetic disorder caused by mutations in the protein C gene (PROC). More than 10% of nonsense and frameshift mutations carrying premature termination codons have been identified in PROC, but the exact molecular mechanisms of these mutations on the pathogenesis of protein C deficiency remain unclear. At study enrollment (baseline), patients with and without severe protein C deficiency were similar in age and likelihood of comorbidities. Patients with severe protein C deficiency had lower arterial blood pressure (P = .0006), greater serum creatinine concentration (P ¡ .0001), elevated markers of thrombosis and inflammation, and impairment of fibrinolysis (P ¡ .0001). T...

Context of the Advance RAG: Physical findings vary amongst patients but it is common to find pelvic and endocrine as well as skin changes. These include changes associated with underlying anemia such as pallor and a pale conjunctiva. Endocrine findings such as increased hair growth, clitoromegaly and acne may help diagnose underlying endocrine related causes of abnormal bleeding. In those experiencing uterine bleeding due to coagulopathies, signs of platelet deficiencies may be present, such as bruising and petechiae

Option D: Von Willebrand disease
Context of the initial RAG: Type IIH von Willebrand disease was reported 20 years ago as a novel variant characterized by the loss of the largest multimers in plasma and platelets and absence of the typical triplet structure. Tests that may be done to diagnose this disease include: Bleeding time (is prolonged) Platelet aggregation test Platelet count (may be low or normal) Ristocetin cofactor test (the primary assay test used to diagnose von Willebrand disease) Von Willebrand factor level (level is reduced) This disease may also alter the results of the following tests: Factor VIII level Von Willebrand factor multimers (parts of the von Willebrand factor protein molecule) Von Willebrand disease may be hard to diagnose....

Context of the Advance RAG: Problems with coagulation may dispose to hemorrhage, thrombosis, and occasionally both, depending on the nature of the pathology. Platelet conditions may be inborn or acquired. Some inborn platelet pathologies are Glanzmann's thrombrasthenia, Bernard-Soulier syndrome (abnormal glycoprotein Ib-IX-V complex), gray platelet syndrome (deficient alpha granules) and delta storage pool deficiency or delta dense gran

A.6 Question

Question: A 40-year-old zookeeper presents to the emergency department complaining of severe abdominal pain that radiates to her back, and nausea. The pain started 2 days ago and slowly increased until she could not tolerate it any longer. Past medical history is significant for hypertension and hypothyroidism. Additionally, she reports that she was recently stung by one of the zoo's smaller scorpions, but did not seek medical treatment. She takes aspirin, levothyroxine, oral contraceptive pills, and a multivitamin daily. Family history is noncontributory. Today, her blood pressure is 108/58 mm Hg, heart rate is 99/min, respiratory rate is 21/min, and temperature is 37.0°C (98.6°F). On physical exam, she is a well-developed, obese female that looks unwell. Her heart has a regular rate and rhythm. Radial pulses are weak but symmetric. Her lungs are clear to auscultation bilaterally. Her lateral left ankle is swollen, erythematous, and painful to palpate. An abdominal CT is consistent with acute pancreatitis. Which of the following is the most likely etiology for this patient's disease?

Option A: Aspirin
Context of the initial RAG: Aspirin is considered one of the most prescribed drugs worldwide, predominantly for its cardioprotective effects. However, its use may be pre-

cluded by gastrointestinal and haematological side-effects. Patients received an intravenous infusion of 250 mg aspirin. A cross-sectional design was used, and data collected from 2008 to 2010. Regular aspirin use (aspirin therapy) was defined as taking aspirin most days of the week. We found 831 individuals for whom complete data were available for regression analyses and stratified the sample into 2 groups: those for whom aspirin therapy was indicated and those for whom it was not indicated, based on national guidelines....

Context of the Advance RAG: Scorpion envenomation may be accompanied by metabolic acidosis even in the absence of hypoxia and cardiovascular derangement. We tested the hypothesis that venom causes ischemia of the gastrointestinal tract rather than failure of delivery of oxygen to the periphery. Repeated measures, prospective study in experimental animals. University-affiliated hospital research laboratory. In ten spontaneously breathing, intubated, sedated pigs, purified dried venom (Leiurus quinquestriatus), 0

Option B: Oral contraceptive pills
Context of the initial RAG: Healthy volunteers using the combined oral contraceptive pill. Among 206 women, 86 were at risk for unplanned pregnancy. Most (59%) had not received contraceptive counseling in the last year, 22% reported inconsistent contraceptive use, and 53% depended solely on barrier methods. Intrauterine device contraceptives (IUDs) were used by 13%. Women using potentially teratogenic medications were no more likely to have received contraceptive counseling, to have used contraception consistently, or to have used more effective contraceptives. A history of thrombosis or aPL did not account for low rates of hormonal methods. Four women with a history of thrombosis or aPL were using estrogen-containing ...

Context of the Advance RAG: Tachycardia may be present due to pain, anxiety, aortic rupture with massive bleeding, pericardial tamponade, arapic insufficiency with acute pulmonary edema and hypoxemia. Pulsus paradoxus (a drop of ¿ 10 mmHg in arterial blood pressure on the left side of the body, and a drop of ¡ 10mmHg on the right side) is a grave prognostic indicator. A wide pulse pressure

Option C: Scorpion sting
Context of the initial RAG: We describe the epidemiology and clinical features of scorpion stings presenting to an emergency department in Singapore, including that of the venomous species Isometrus maculatus. A management approach to scorpion stings is proposed. To study the clinical aspects and frequency of scorpion stings in Riyadh region of Saudi Arabia. A total of 391 cases of scorpion stings were recorded from the 2-referral hospitals, 248 (63.4%) of were men and 143 (36.6%) were women. The 21-30 years age group was the worst affected, followed by 31-40 years, 11-20 years, and ¡10 years age groups. Larger number of stings occurred during the summer months, at nights, and on distal limbs. Most of the patients reac...

Context of the Advance RAG: Hyperglycemia has been described in severe scorpion envenomation, we wanted to analyze if it was applicable to viper bites in children. To describe clinical, biological, and therapeutic characteristics of 83 children bitten by European viper (Vipera spp.) and to confirm that hyperglycemic is a risk factor for

high-grade envenoma. A retrospective study was conducted between 2001 and 2014 in the pediatric emergency department of a tertiary level children's hospital

Option D: Hypothyroidism
Context of the initial RAG: Prospective study of patients with chemically confirmed overt hypothyroidism. Fifty consecutive newly diagnosed, untreated symptomatic patients with primary hypothyroidism (age: 34+/-11 years; males: 21 [42%]) were prospectively studied. Physical examination, anthropometry, fasting blood glucose and serum lipids were performed in all patients at baseline. Polysomnography was done at baseline in all patients and was repeated after adequate thyroxine replacement in those who had SDB. Retrospective review of 21 children (10.1 +/- 3.0 years) with profound hypothyroidism....

Context of the Advance RAG: proptosis may cause corneal exposure and damage, especially if the lids fail to close during sleep. Periorbital edema, scleral injection, and chemosis are also frequent. In 5–10% of patients, the muscle swelling is so severe that diplopia results. The most serious manifestation is compression of the optic nerve at the apex of the orbit, leading to papilledema, peripheral field defects, and permanent loss of vision if left untreated

A.7 Question

Question: A 25-year-old primigravida presents to her physician for a routine prenatal visit. She is at 34 weeks gestation, as confirmed by an ultrasound examination. She has no complaints, but notes that the new shoes she bought 2 weeks ago do not fit anymore. The course of her pregnancy has been uneventful and she has been compliant with the recommended prenatal care. Her medical history is unremarkable. She has a 15-pound weight gain since the last visit 3 weeks ago. Her vital signs are as follows: blood pressure, 148/90 mm Hg; heart rate, 88/min; respiratory rate, 16/min; and temperature, 36.6℃ (97.9). The blood pressure on repeat assessment 4 hours later is 151/90 mm Hg. The fetal heart rate is 151/min. The physical examination is significant for 2+ pitting edema of the lower extremity. Which of the following tests o should confirm the probable condition of this patient?

Option A: Bilirubin assessment
Context of the initial RAG: We examined sequential sera from 72 patients with serum bilirubin greater than 5 mg/dl. Total bilirubin level in the control group was significantly higher than those of the other groups. After multivariable linear regression analysis total bilirubin [=-3.131 (-4.481, -1.782), p¡0.001] was significantly associated with the severity of CAD. Futhermore, there was a moderate and significant inverse correlation between serum total bilirubin level and the severity of CAD (r=-0.173, p¡0.001), CRP (r=-0.112, p¡0.001), NLR (r=-0.070, p=0.026) and RDW (r=-0.074, p=0.027). Twenty-five patients (18 females and 7 males) were enrolled in the study group. The control group included 44 patients (26 female...

Context of the Advance RAG: To assess the relationship between blood pressure pattern and intrauterine growth restriction in normotensive pregnant women. Twenty-four-hour ambulatory blood pressure was consecutively performed between 32 and 34 weeks in 139 normotense, non-proteinuric, primigravidae with intrauterines growth restriction (IUGR) and in 140 primigraveidae, matched for age and gestation, who were and remained normotensible throughout pregnancy and whose fetuses had regular fetal growth

Option B: Coagulation studies
Context of the initial RAG: Coagulation tests. Twenty units of FFP, five units of each blood group A, B, AB, and O, were thawed, and aliquots were taken for measurement of coagulation factors. The plasma units were then kept for 24 hours at 4 degrees C, at which point a second aliquot was taken, The remaining FFP units were refrozen and kept at -80 degrees C for 1 week. The above procedure was then repeated. Coagulation-factor activity and fibrinogen level were measured by the coagulation analyzer. To determine the effect of citrate concentration (3.2 vs 3.8%) on coagulation tests in dogs....

Context of the Advance RAG: To determine the extent to which fetal weight during mid-pregnancy and fetal weight gain were associated with higher body mass index (BMI) z-scores at age 3 years, we analyzed the relationship between fetal weight, weight, subscapular and triceps skinfold thicknesses, and BP at age3 years. Among 438 children in the Project Viva cohort, we estimated fetal weight at 16-20 (median 18) weeks' gestation using ultrasound biometry measures

Option C: Leukocyte count with differential
Context of the initial RAG: The aim of this study was to validate differential leukocyte counts in blood from chickens using the Cell-Dyn 3500 hematology system and avian-specific software. Determination of leukocyte (WBC) counts in pleural fluid is routinely performed by microscopic examination. In this study, we evaluated the performance of automated (differential) WBC counting in comparison with manual counting. Groups A and B did not differ in leukocyte counts and the differences between groups B and C were restricted to single time points. Neither groups A and B, nor groups B and C differed significantly in the relative distribution of lymphocyte subpopulations or in the percentage of CD126+, HLA-DR+, CD45 RO+ and...

Context of the Advance RAG: and 8.6, 95% CI 2.9-25, respectively), while that of PlGF 0.396 MoM had the lowest likelihood ratio of a positive test (0.08, 95%; CI 0.03-0.25). The association between low plasma concentrations of Pl GF/sVEGFR-1 (0.05 MoM) as well as that of plGF/sEng (0.07 MoM), and

Option D: 24-hour urine protein
Context of the initial RAG: Women requiring a baseline evaluation for proteinuria supplied a urine sample the morning after their 24-hour collection. The PCR was analyzed as a predictor of significant proteinuria (150mg). A regression equation to estimate the 24-hour protein value from the PCR was then developed. Proteinuria in the studied patients was assessed by 24-hour protein excretion (24-hour PRT) and spot urine P/Cr ratio. The analysis of concordance between 24-hour PRT and P/Cr was carried out using intraclass correlation coefficient (ICC), paired t-test and Bland-Altman plots. The discriminant cutoff values for spot urine P/Cr ratio in predicting 24-hour protein

"threshold" excretion were determined using re...

Context of the Advance RAG: Our purpose was to investigate the effect of proteinuria associated with pre-eclampsia on intrapartum fetal heart rate (FHR) monitoring. A retrospective study was performed involving 79 pregnant women with post-eccentricular hypertension (GH) at delivery and 79 women with low-risk pregnancies and GH (GH and mild UP). The women were classified into two groups according to their gestational age and gestational weight. The women with GH and GH were classified as

A.8 Question

Question: A 3900-g (8.6-lb) male infant is delivered at 39 weeks' gestation via spontaneous vaginal delivery. Pregnancy and delivery were uncomplicated but a prenatal ultrasound at 20 weeks showed a defect in the pleuroperitoneal membrane. Further evaluation of this patient is most likely to show which of the following findings?

Option A: Gastric fundus in the thorax
Context of the initial RAG: The primary aim of this study was to test the widespread assumption that the viability of the gastric fundus is compromised by fundoplication, thereby limiting the use of stomach to reconstruct the upper gastrointestinal tract after esophageal resection. We performed sleeve gastrectomies on 11 cadaveric trunks with a detailed anatomical study of the gastric vascular supply after latex injection in the three branches arising from the celiac trunk. The patient had been in an intensive weight loss programme for several years, but within the last 12 months her body weight had increased again dramatically. At referral she presented with a body mass index (BMI) of 43.1 kg/m(2) (height 169 cm, preo...

Context of the Advance RAG: Our objective was to compare neonatal postoperative morbidity for the neonate with prenatally diagnosed gastroschisis delivered vaginally with that for the perinatal neonates undergoing elective cesarean at or before the onset of labor. Retrospective maternal and neonatal data were obtained by chart review on 22 neonates prenatal diagnosed with gastros chisis who underwent operative closure of the ventral wall defect between 1987 and 1991 at Loma Linda University

Option B: Pancreatic ring around the duodenum
Context of the initial RAG: A gross photograph of liver and pancreas from the autopsy. The pancreas is slightly smaller than normal and it has a mucous consistency. This section of duodenum demonstrates dilation, loss of rugae, and areas of ulceration (arrows). Duodenal diverticula are common incidental findings. Although a definite treatment is rarely required, an association with biliary and pancreatic diseases is often suggested. Our aim was to determine the frequency of complications in relation to the location of the diverticulum. The celiac artery and its branches; the stomach has been raised and the peritoneum removed. Superior and inferior duodenal fossæ. Duodenojejunal fossa. Interior of the stomach. Section o...

Context of the Advance RAG: Duodenum starts developing during the 6th and 7th week of gestation. Re-canalization occurs during the 8th to 10th week. It is thought that duodenal atresia is the result of failure of re-calization of the duodenum in 8 to 10 weeks of fetal development. This is due to failure of neural cell migration Gastroschisis (GS) is usually described as an abdominal wall defect, to the right of

Option C: Hypertrophy of the gastric pylorus
Context of the initial RAG: Gastric mucosal biopsies from the antrum and the corpus of the stomach were cultured. H. pylori status was determined by histological assessment using the Genta stain. To explore the mechanism by which H pylori causes activation of gastric epithelial cells. Although pylorus-preserving gastrectomy (PPG) is performed as a function preserving surgery, patients sometimes suffer from postoperative stasis of the gastric contents after the procedure. Preservation of blood flow and both celiac and pyloric branches of the vagal nerve may decrease the incidence of the stasis....

Context of the Advance RAG: Infantile hypertrophic pyloric stenosis (IHPS) is a common condition which presents in infants at 2-12 weeks of postnatal life, and whose cause remains obscure. Multiple associated abnormalities have been recognized within the external hypertrophied pylori muscle layer, but the internal component of the pylorus mucosa has received scant attention in the literature to date. Our purpose in this study was to show that pyloria mucosal redundancy is a constant finding

Option D: Large bowel in the inguinal canal
Context of the initial RAG: Of 266 consecutive adult patients with partial small-bowel obstruction admitted at a tertiary medical center, 236 were randomized into 2 groups. Group I patients were treated with intravenous hydration, nasogastric tube decompression, and NPO. Group II patients were placed on intravenous hydration, nasogastric tube decompression, and oral fluids incorporating an oral laxative, a digestant, and a defoaming agent. We compared differences between the groups in (1) the number of patients having a successful nonoperative treatment, (2) complications, and (3) recurrence of symptoms. CT and MRI scans are useful for evaluating the small bowel with enteroclysis protocols Restorative ileal pouch-anal ...

Context of the Advance RAG: Extensive intestinal surgery in very preterm infants and its influence on somatic growth is of major concern. There is little consensus as to which is the most appropriate surgical approach in extremely low-birth-weight infants with abdominal pathology. Laparotomy is currently advocated, but peritoneal drainage is also discussed. To study laparotomy as surgical intervention in newborn infants with less than 28 gestational weeks and to investigate associated mortality and morbidity and its impact on short-term growth.

A.9 Question

Context of the initial RAG: A 62-year-old woman presents for a regular check-up. She complains of lightheadedness and palpitations which occur episodically. Past medical history is significant for a myocardial infarction 6 months ago and NYHA class II

chronic heart failure. She also was diagnosed with grade I arterial hypertension 4 years ago. Current medications are aspirin 81 mg, atorvastatin 10 mg, enalapril 10 mg, and metoprolol 200 mg daily. Her vital signs are a blood pressure of 135/90 mm Hg, a heart rate of 125/min, a respiratory rate of 14/min, and a temperature of 36.5°C (97.7°F). Cardiopulmonary examination is significant for irregular heart rhythm and decreased S1 intensity. ECG is obtained and is shown in the picture (see image). Echocardiography shows a left ventricular ejection fraction of 39%. Which of the following drugs is the best choice for rate control in this patient?

Option A: Atenolol
Context of the initial RAG: Ambulatory surgical patients on long-term atenolol or metoprolol. To evaluate the perioperative use of atenolol in reducing the incidence of hematoma after rhytidoplasty. The role of atenolol, a non-vasodilating beta-blocker drug, on long-term mortality in hypertensive older adults is still unclear. The aim of the present study was to evaluate long-term mortality in community-dwelling hypertensive older adults taking atenolol....

Context of the Advance RAG: Reduced heart rate variability (HRV) has been shown to predict mortality in heart failure (CHF). The relationship between improved cardiac function and improvement in HRV has not been previously studied. This was substudy of a randomized, placebo-controlled, double-blinded trial of carvedilol of four months duration. Analysis of HRV was performed on 24-hour Holter monitors obtained at baseline and completion of study. All subjects had symptomatic CHF and an left

Option B: Diltiazem
Context of the initial RAG: To assess the long-term results of management with diltiazem 2% ointment using a telephone questionnaire. Ten healthy male volunteers were included in a randomised, open, crossover study, comparing the effect of a single oral dose of non-retard formulated diltiazem (120 mg) administered with 250 ml grapefruit juice or water. The study was performed on two investigation days separated by 13-38 days (median 28 days). Plasma samples were collected for measurement of diltiazem and the metabolites MA and M1. Blood pressure and heart rate were monitored throughout the study. A descriptive, retrospective study from March 2004 to March 2011 in patients with CAF on diltiazem 2%, 3 applications daily ...

Context of the Advance RAG: Begin therapy with either a beta blocker, diltiazem, or verapamil (class I, level of evidence B). Use a combination of digoxin and either aBeta blocker, Diltiazepamil if AF is not controlled by monotherapy (class IIa, Level of evidence A). Consider ablation of the arterioventricular (AV) node or accessory pathway if pharmacological therapy is insufficient (class 2a). If rate is not determined by the

Option C: Propafenone
Context of the initial RAG: Propafenone is a well-known Class Ic antiarrhythmic agent. It has the typical chemical structure of a beta-blocker, but human studies on its beta-blocking effects revealed conflicting results. Talk to your doctor about your diet. Foods and salt substitutes containing potassium can affect the action of propafenone. Propofol (10...

Context of the Advance RAG: scan quality interpretatrion Clinical instability (acute respiratory distress, severe hypotension, unstable arrhythmia) Severe symptomatic aortic stenosis Significant hypotension (SBP ¡90 mm Hg) Respiratory failure Severe COPD, acute pulmonary embolism, severe pulmonary hypertension Significant claustrophobia Renal impairment Severe systemic arterial hypertension (200/110 mmHg) Known or suspected bronchoconstriction or bron

Option D: Digoxin
Context of the initial RAG: The indications of digoxin therapy has been significantly narrowed and also the effective target therapeutic blood level has been decreased (0.9 micromol/L) compared to the previously desired one. This study sought to examine the hemodynamic and autonomic dose response to digoxin. This was a prospective observational study over 9 months, set in two general medical wards. We studied consecutive patients (n = 141) who were receiving digoxin. Measurements included digitalis toxicity, defined by ECG criteria and resolution after stopping digoxin; all additional medications (including antiarrhythmics) continued. The observer was "blinded" to serum digoxin level and to concomitant drugs....

Context of the Advance RAG: Keep all appointments with your doctor and the laboratory. Your doctor will need to determine your response to digoxin. You may have electrocardiograms (EKGs) and blood tests periodically, and your dose may need to be adjusted.Your doctor may ask you to check your pulse (heart rate). Ask your pharmacist or doctor to teach you how to take your pulse. If your pulse is faster or slower than it should be, call your doctor. Do not let anyone else

A.10 Question

Context of the initial RAG: A 35-year-old male presents to his primary care physician with complaints of seasonal allergies. He has been using intranasal vasoconstrictors several times per day for several weeks. What is a likely sequela of the chronic use of topical nasal decongestants?

Option A: Epistaxis
Context of the initial RAG: This study aims to discuss the management and the follow-up approach in patients with epistaxis. All patients with a diagnosis of epistaxis who were admitted for in-patient care at six ENT departments between November 2011 and February 2012 were prospectively enrolled. A total of 367 patients with epistaxis (209 males, 158 females; mean age 52.6±18.3 years; range 18 to 85 years) admitted to the Adult Emergency Department of a university hospital between January 2000 and December 2004 were retrospectively analyzed....

Context of the Advance RAG: Mucosal ulcers and perforations of the nasal septum are very rare and may have several underlying causes. Contact allergy to steroids has been suggested as a possible aetiological factor in patients who develop perforation

during topical steroid use. We have identified 13 subjects with perforating of their nasal septicum and concomitant topical nasal steroid use in order to evaluate whether these patients had developed contact allergy to the steroids they underwent patch testing with an extended steroid series

Option B: Permanent loss of smell
Context of the initial RAG: Short-term exposure to odours, also called "olfactory training" has been shown to improve olfactory function in healthy people but also in people with olfactory loss. Aim of this single center, prospective, controlled study was to investigate the change of olfactory function following twice-daily, short-term exposure to 4 odours over a period of approximately 12 weeks. Prevalence and incidence of smell disturbance; adjusted odds ratios and 95% confidence intervals (CIs) of associated conditions and medications. Patients with PER and subjective loss of the sense of smell (n = 27) were included in this pilot randomised, double-blind, placebo-controlled study. Nasal symptoms, nasal endoscopy, s...

Context of the Advance RAG: To understand the mechanism underlying the nasal congestive response to irritant challenge. We exposed 22 subjects–8 with seasonal allergic rhinitis (SAR), 6 with perennial allergic rhinusitis (PAR), and 8 normals–to chlorine (Cl2) gas (1.0 ppm x 15 min.) by nasal CPAP mask. Control exposures (filtered air) were carried out on separate days, with counter-balancing of exposure order. Nasal airway resistance (

Option C: Persistent nasal crusting
Context of the initial RAG: Mucosal ulcers and perforations of the nasal septum are very rare and may have several underlying causes. Contact allergy to steroids has been suggested as a possible aetiological factor in patients who develop perforations during topical steroid use. To understand the mechanism underlying the nasal congestive response to irritant challenge. Nasal mucosa from 10 normal individual and 4 patients of nasal polyps were studied with immunohistochemical technique and histopathologic examination....

Context of the Advance RAG: Fluticasone propionate aqueous nasal spray, a new topical corticosteroid preparation, is effective when given as 200 micrograms once daily in patients (¿ 12 years of age) with seasonal allergic rhinitis. To evaluate the efficacy and safety of fluticasion proprionate, we conducted a randomized, double-blind, placebo-controlled, parallel-group. Two hundred fifty children aged 4 to 11 years were randomly assigned to receive flutic

Option D: Persistent congestion
Context of the initial RAG: We tested the hypothesis that passive congestion is more important than poor perfusion. We measured serum creatinine levels on a daily basis during the hospitalization and assessed the persistence of signs of congestion at discharge in 599 consecutive patients admitted at our institute for AHF. They had a postdischarge mortality and mortality or AHF readmission rates of 13% and 43%, respectively, after 1 year. Patients were subdivided into 4 groups according to the development or not of WRF and the persistence of 1 sign of congestion at discharge. Patients with WRF and no congestion had similar outcomes compared with those with no WRF and no congestion,

whereas the risk of death or of death...

Context of the Advance RAG: A recent survey estimated that 85% of patients with allergic rhinitis experience nasal congestion. This symptom considerably impacts quality of life. To evaluate the effectiveness of mometasone furoate nasal spray (MFNS) in subjects with seasonal allergic rhinusitis (SAR) experiencing moderate-to-severe nasal congestion, we conducted a randomized, double-blind, placebo-controlled studies of MFNS 200 microg once daily in patients with SAR. Subject-evaluated nasal congestion

A.11 Question

Question: A 46-year-old woman comes to the physician because of a 2-week history of diplopia and ocular pain when reading the newspaper. She also has a 3-month history of amenorrhea, hot flashes, and increased sweating. She reports that she has been overweight all her adult life and is happy to have lost 6.8-kg (15-lb) of weight in the past 2 months. Her pulse is 110/min, and blood pressure is 148/98 mm Hg. Physical examination shows moist palms and a nontender thyroid gland that is enlarged to two times its normal size. Ophthalmologic examination shows prominence of the globes of the eyes, bilateral lid retraction, conjunctival injection, and an inability to converge the eyes. There is no pain on movement of the extraocular muscles. Visual acuity is 20/20 bilaterally. Neurologic examination shows a fine resting tremor of the hands. Deep tendon reflexes are 3+ with a shortened relaxation phase. Which of the following is the most likely cause of this patient's ocular complaints?

Option A: Granulomatous inflammation of the cavernous sinus
Context of the initial RAG: We studied nonfunctioning pituitary adenomas extending to the cavernous sinus to gain insight into the discrepancy between their histologically benign nature and frequent extension into the cavernous sinus. Allergic fungal rhino sinusitis (AFS) is classically described as allergic manifestation to the fungal antigen present in sinuses with no evidence of invasion. Granulomas in histopathology, suspicious of invasion, are occasionally observed in AFS and the disease in these patients behaves like invasive fungal sinusitis even without histologic evidence of invasion. We retrospectively studied AFS patients to analyze whether AFS should be continued to be designated as an allergic entity. To i...

Context of the Advance RAG: This is a common occurrence for several CED patients, often causing myopathy and extensive sleep deprivation from the chronic disabling pain. Patients may even require the use of a wheelchair, especially after being bedridden or housebound for days or weeks at a time.'Flare-ups' may be attributed to, or exacerbated by illness, stress, exhaustion, infection, exercise, standing or walking for too long, cold weather, electrical storms, and sudden changes in barometric pressure. Engelmann

Option B: Abnormal communication between the cavernous sinus and the internal carotid artery
Context of the initial RAG: In human anatomy, the carotid sinus is a localized di-

lation of the internal carotid artery at its origin, the common carotid artery bifurcation. The cavernous sinus had four walls, namely medial, lateral, posterior and superior walls. Five venous spaces within the sinus were identified by their relation to the carotid artery; those were the medial, lateral, posterosuperior, posteroinferior and anterolateral compartments. Three branches arising from the cavernous segment of internal carotid artery from proximal to distal were meningohypophyseal trunk, inferolateral trunk and McConnell capsular artery. Cavernous sinuses communicated each other by intercavernous sinuses, as well as basilar sinu...

Context of the Advance RAG: movement of the neck, wearing of a tight collar, shaving, etc. This history is not necessary, however, to make the diagnosis. Patients are usually upright, often standing, and develop a sudden episode of syncope, often with an associated fall. Small convulsive movements often occur with the loss of consciousness. The loss of sight is usually ¡30 seconds, and patients awake quickly with no clouding of consciousness, the syndrome has been described in patients in chronic Afib,

Option C: Glycosaminoglycan accumulation in the orbit
Context of the initial RAG: Cell surface proteoglycans play vital functional roles in various biological processes such as cell proliferation, differentiation, adhesion, inflammation, immune response, sustentation of cartilage tissue and intensity of tissues. We show here that serglycin-like synthetic glycopeptides function efficiently as a molecular shuttle to hijack glycosaminoglycan (GAG) biosynthetic pathway within cells across the plasma membrane. In the present study, we have investigated the first step of the cellular uptake mechanism of MPG and shown that both MPG and MPG-cargo complexes interact with the extracellular matrix through the negatively charged heparan sulfate proteoglycans. We demonstrated that ini...

Context of the Advance RAG: To investigate the effects of combined orbital bone and fat decompression on intraocular pressure (IOP) and superior ophthalmic vein blood flow velocity (SOV-BFV), and their association with the clinical features of inactive eye disease (GO), we investigated the effect of orbital decompression in patients with moderate-to-severe orbitopathy (GO). During the 2002-2008 period, 72 eyes of 36 GO cases demonstrating moderate to severe orbitopathy were evaluated according to their clinical features

Option D: Sympathetic hyperactivity of levator palpebrae superioris
Context of the initial RAG: The aim of the present study was to assess whether sympathetic hyperactivity contributes to an altered chemosensory function in ESRD. Three accessory levator muscle slips of the levator palpebrae superioris muscle were identified. One of these arose laterally from the origin of the levator palpebrae superioris muscle. At its anterior end, it divided into two parts, the main superior and a smaller inferior accessory. The second had an accessory levator fibromuscular slip. It arose medially from the origin of the levator palpebrae superioris and lost its muscular character after a short course. The third arose from the origin of the levator palpebrae superioris as a thin flat muscle. Sympathet...

Context of the Advance RAG: The etiology of third nerve palsy is usually diagnosed by history, motility examination, and presence of lid and pupil involvement, as well

as cranial and vascular imaging. We used high-resolution magnetic resonance imaging (hrMRI) of the oculomotor nerve and affected extraocular muscles (EOMs) to investigate oculOMotor palsy. Prospective, noncomparative, observational case series in an academic referral setting. Twelve patients with nonaneurys

A.12 Question

Question: A 1-year-old boy presents to the emergency department with weakness and a change in his behavior. His parents state that they first noticed the change in his behavior this morning and it has been getting worse. They noticed the patient was initially weak in his upper body and arms, but now he won't move his legs with as much strength or vigor as he used to. Physical exam is notable for bilateral ptosis with a sluggish pupillary response, a very weak sucking and gag reflex, and shallow respirations. The patient is currently drooling and his diaper is dry. The parents state he has not had a bowel movement in over 1 day. Which of the following is the pathophysiology of this patient's condition?

Option A: Autoantibodies against the presynaptic voltage-gated calcium channels
Context of the initial RAG: SKF96365 (SKF), originally identified as a blocker of receptor-mediated calcium entry, is widely used diagnostically, as a blocker of transient receptor potential canonical type (TRPC) channels. While SKF has been used as a tool to define the functional roles of TRPC channels in various cell and tissue types, there are notable overlapping physiological and pathophysiological associations between TRPC channels and low-voltage-activated (LVA) T-type calcium channels. The activity of SKF against T-type Ca channels has not been previously explored, and here we systematically investigated the effects of SKF on recombinant and native voltage-gated Ca channel-mediated currents. Canonical transient ...

Context of the Advance RAG: The excessive amounts of adrenal testosterone produce little effect on the genitalia of male infants with severe CAH. If a male infant with CAH is not detected by newborn screening, he will appear healthy and normal and be quickly discharged home to his family. However, the lack of aldosterone results in a high rate of sodium loss in the urine. Urinary sodium concentrations may exceed 50 mEq/L. With this rate of salt loss, the infant cannot maintain blood volume

Option B: Autoimmune demyelination of peripheral nerves
Context of the initial RAG: Archival tissue samples derived from patients with pathologically confirmed central nervous system inflammatory demyelinating disease who had undergone either diagnostic serial biopsy or biopsy followed by autopsy were analyzed immunohistochemically. The inclusion criteria consisted of the presence of early active demyelinating lesions–required for immunopattern classification–obtained from the same patient at 2 or more time points. To present the clinical, electrophysiologic, radiologic, and pathologic features of six patients with an asymmetric sensory or sensorimotor demyelinating neuropathy. All six patients were initially affected in only one limb; in four patients the neuropathy prog...

Context of the Advance RAG: Ptosis and strabismus are 2 common presenting complaints of preschool-age patients. In both cases, these conditions can be benign and require no further workup. However, sudden onset of these findings can indicate a more serious neurologic problem. If a patient presents with multiple neurologic signs, a sudden onset eye turn, or ptosis, the patient must undergo a workup to rule out a pathologic etiology, specifically a brain tumor. The workup should include

Option C: Blockade of presynaptic acetylcholine release at the neuromuscular junction
Context of the initial RAG: The turnover of acetylcholine receptors at the neuromuscular junction is regulated in an activity-dependent manner. Upon denervation and under various other pathological conditions, receptor half-life is decreased. Various protein kinase C (PKC) isoforms contribute to the phosphorylating activity that modulates neurotransmitter release. In previous studies we showed that nPKC is confined in the presynaptic site of the neuromuscular junction and its presynaptic function is activity-dependent. Furthermore, nPKC regulates phorbol ester-induced acetylcholine release potentiation, which further indicates that nPKC is involved in neurotransmission. The present study is designed to examine the n...

Context of the Advance RAG: The health care provider will take a medical history, which includes strength and endurance. A physical examination of strength shows weakness, often beginning in one area. There may be muscle tremors, spasms, twitching, or loss of muscle tissue (atrophy). Atrophy and twitching of the tongue are common. The person's walk may be stiff or clumsy. Reflexes are abnormal. There are increased reflexes at the joints, but there may be a loss of the gag

Option D: Lower motor neuron destruction in the anterior horn
Context of the initial RAG: To determine possible hemispheric differences of motor imagery in facilitating the anterior horn cells. An upper motor neuron lesion is a lesion of the neural pathway above the anterior horn cell or motor nuclei of the cranial nerves. This is in contrast to a lower motor neuron lesion, which affects nerve fibers traveling from the anterior horn of the spinal cord to the relevant muscle(s). To determine whether upper motor neuron lesions in stroke can cause transneuronal degeneration of lower motor neurons, we assessed spinal anterior horn cells in patients dying with poststroke hemiplegia....

Context of the Advance RAG: to have fine or gross motor difficulties and dysdiadochokinesia. Orange colored crystals in diapers Nephrolithiasis Gouty arthritis Developmental delay: evident by 3- 6 months of age. Decreased muscle tone (hypotonia) Difficulty crawling or walking Lack of speech is also a very common trait associated with LNS. Irritability Extrapyramidal involvement: Abnormal involuntary muscle contractions Loss of motor control, Writhing motions, Arching of