

Performance of large language models on advocating the management of meningitis: a comparative qualitative study

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ABSTRACT

Objectives We aimed to examine the adherence of large language models (LLMs) to bacterial meningitis guidelines using a hypothetical medical case, highlighting their utility and limitations in healthcare.

Methods A simulated clinical scenario of a patient with bacterial meningitis secondary to mastoiditis was presented in three independent sessions to seven publicly accessible LLMs (Bard, Bing, Claude-2, GTP-3.5, GTP-4, Llama, PaLM). Responses were evaluated for adherence to good clinical practice and two international meningitis guidelines.

Results A central nervous system infection was identified in 90% of LLM sessions. All recommended imaging, while 81% suggested lumbar puncture. Blood cultures and specific mastoiditis work-up were proposed in only 62% and 38% sessions, respectively. Only 38% of sessions provided the correct empirical antibiotic treatment, while antiviral treatment and dexamethasone were advised in 33% and 24%, respectively. Misleading statements were generated in 52%. No significant correlation was found between LLMs' text length and performance ($r=0.29$, $p=0.20$). Among all LLMs, GTP-4 demonstrated the best performance.

Discussion Latest LLMs provide valuable advice on differential diagnosis and diagnostic procedures but significantly vary in treatment-specific information for bacterial meningitis when introduced to a realistic clinical scenario. Misleading statements were common, with performance differences attributed to each LLM's unique algorithm rather than output length.

Conclusions Users must be aware of such limitations and performance variability when considering LLMs as a support tool for medical decision-making. Further research is needed to refine these models' comprehension of complex medical scenarios and their ability to provide reliable information.

INTRODUCTION

Large language models (LLMs) are powerful artificial intelligence (AI) models trained on extensive text data to generate human-like text. They can interpret user-generated textual instructions (prompts) and respond immediately with the contextually most appropriate response based on probabilistic

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Large language models (LLMs) have demonstrated proficiency in responding to medical licensing examination-level queries and shown aptitude in accurate medical triage decision-making. However, performance with knowledge-testing scenarios is not necessarily indicative of effectiveness in real-world medical contexts.

WHAT THIS STUDY ADDS

⇒ This investigation presents a qualitative analysis of the performance of seven publicly accessible LLMs, using a stepwise presentation of a hypothetical bacterial meningitis case reflecting a real-world scenario. While LLMs generally offered helpful triage and diagnostic advice, there were significant discrepancies in their recommendations for treatment and specific diagnostic work-ups. Moreover, the generation of misleading statements and variability in performances between different sessions were observed among individual LLMs.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights the current capabilities of LLMs in handling real-world medical emergency situations and identifies areas of future research, such as enhancing LLMs' understanding of complex medical scenarios and their capacity for delivering reliable and deterministic information.

computations learnt during their training. Lately, several LLMs were released to the public, attracting substantial attention for their chat-like interfaces requiring no technical prerequisites.

Recently, both trained and untrained LLMs have shown proficiency in handling medical licensing examination-level questions and demonstrated the ability to make rapid and accurate judgments in medical triage and diagnosing or provide helpful information to patients, underscoring their potential applicability in the healthcare sector.¹⁻⁶ However, the ability to perform well in knowledge-testing

vignettes does not fully reflect the needs of real-world medical settings which demand parallel work-up and nuanced decision-making on the basis of sometimes incomplete information. Considering that physicians already frequently use internet resources for diagnostic decisions and treatment options and that not all hospitals may have free access to the medical literature, it is likely that LLMs will be increasingly used as potential aids in clinical practice.⁷⁻⁹ However, a deeper understanding of their potential and limitations is essential for an appropriate use.¹⁰⁻¹²

This study explored the potentials and limitations of current LLMs by presenting these models with a predefined hypothetical but typical scenario of a patient with acute bacterial meningitis. The aim was to analyse their performance and alignment with good clinical practice and established medical guidelines regarding suggested diagnostic and treatment measures. Bacterial meningitis was chosen for its life-threatening nature, urgency required in diagnosis and treatment and the range of differential diagnoses it involves, making it ideal for assessing the performance of LLMs in a realistic and high stakes medical scenario.

METHODS

Seven publicly accessible LLMs were evaluated between 5 and 8 August 2023: Bard by Google, Bing by Microsoft, generative pre-trained transformer (GTP)-3.5 by OpenAI, GTP-4 by OpenAI (accessed via Poe (Quora)), Claude-2 by Anthropic PBC (accessed via Poe), pathways language model (PaLM) 2 chat-bison-001 by Google (accessed via Poe) and Llama-2-70b by Meta Platforms (accessed via Poe).

Each LLM was presented with the same hypothetical scenario of a patient presenting with symptoms of acute bacterial meningitis (as outlined below) three times within 3 days. The actual diagnosis was not provided. For the LLM Bard, the settings were chosen to inhibit inter-session information storage. All other LLMs claimed that they are incapable of storing user information between sessions. Each session was initiated with a context clearance of previous conversations.

Hypothetical scenario of a patient with acute bacterial meningitis

The patient vignette described a clinical scenario of a patient with acute symptoms due to pneumococcal meningitis secondary to mastoiditis without providing definite diagnosis. The text of the inputted case vignette and the subsequent follow-up queries consisted of five text blocks that were predefined and presented unchanged to each LLM in every session (online supplemental table 1). Given that the performance of LLMs is heavily influenced by prompting,¹³ the initial question began with a contextualisation wherein the LLM was asked to act as an 'experienced medical assistant' and the user was identified as a 'junior medical doctor' seeking advice for a 52-year-old

female patient suffering from severe headache and confusion, followed by an open-ended question about the next steps. This prompt engaged all LLMs in a conversation about the hypothetical case. Second, a detailed vignette was presented, depicting the medical history (notably acute headache and confusion, a history of diabetes type 2 and migraine), vital signs (tachycardia and fever) and prominent abnormal clinical findings (ie, a Glasgow Coma Scale (GCS) of 12 with lethargy, disorientation, fast downward drift of extremities, absence of stiff neck, signs of inflammatory skin of the right mastoid), followed by the open-ended request for a detailed step-by-step recommendation of how to proceed. Third, two closed-ended questions were asked: (1) if a computer tomography (CT) scan of the head needs to be awaited before lumbar puncture (LP) and (2) if administration of antibiotics should be delayed until LP has been performed. Fourth, the exact dosages of antibiotics were asked. Fifth, an open-ended question was asked about any other considerations regarding the treatment or work-up.

The case was created to reflect clinical reality and not a medical license examination question, meaning that information was presented stepwise and reflected a realistic clinical case where not all typical signs and symptoms are necessarily present from the beginning. For example, neck stiffness has shown to have a low sensitivity and as such, its absence cannot rule out meningitis.¹⁴ A search for an infectious focus is crucial and patients should be examined for otitis media or mastoiditis.¹⁵ By this design we aimed to challenge the LLMs in multiple aspects, including good clinical practice, possible differential diagnoses and consideration of risk factors and comorbidities, such as age, diabetes and migraine, for diagnosis and treatment.

Evaluation of LLM performance

The Infectious Diseases Society of America (IDSA) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines were chosen as references as they have previously both been shown in a systematic review to be excellent clinical management guidelines for bacterial meningitis with multinational validity (online supplemental table 2, right column).^{14 16 17}

Individual responses from the LLMs underwent two temporally separated qualitative assessments (accomplished vs unaccomplished) of predefined tasks (online supplemental table 2, middle column) in adherence with good clinical practice and the reference guidelines.¹⁴⁻¹⁸ Accomplished tasks were summarised to a qualitative performance summary. Response consistency was defined as the percentage of responded tasks that were assessed identically (regardless of accomplished or unaccomplished) across all sessions of an individual LLM. In cases where an LLM declined to respond to a question, the corresponding tasks were excluded from the assessment.

As the two reference guidelines differently define criteria for imaging before LP (ie, according to the IDSA guideline, a scan of the brain would be required as

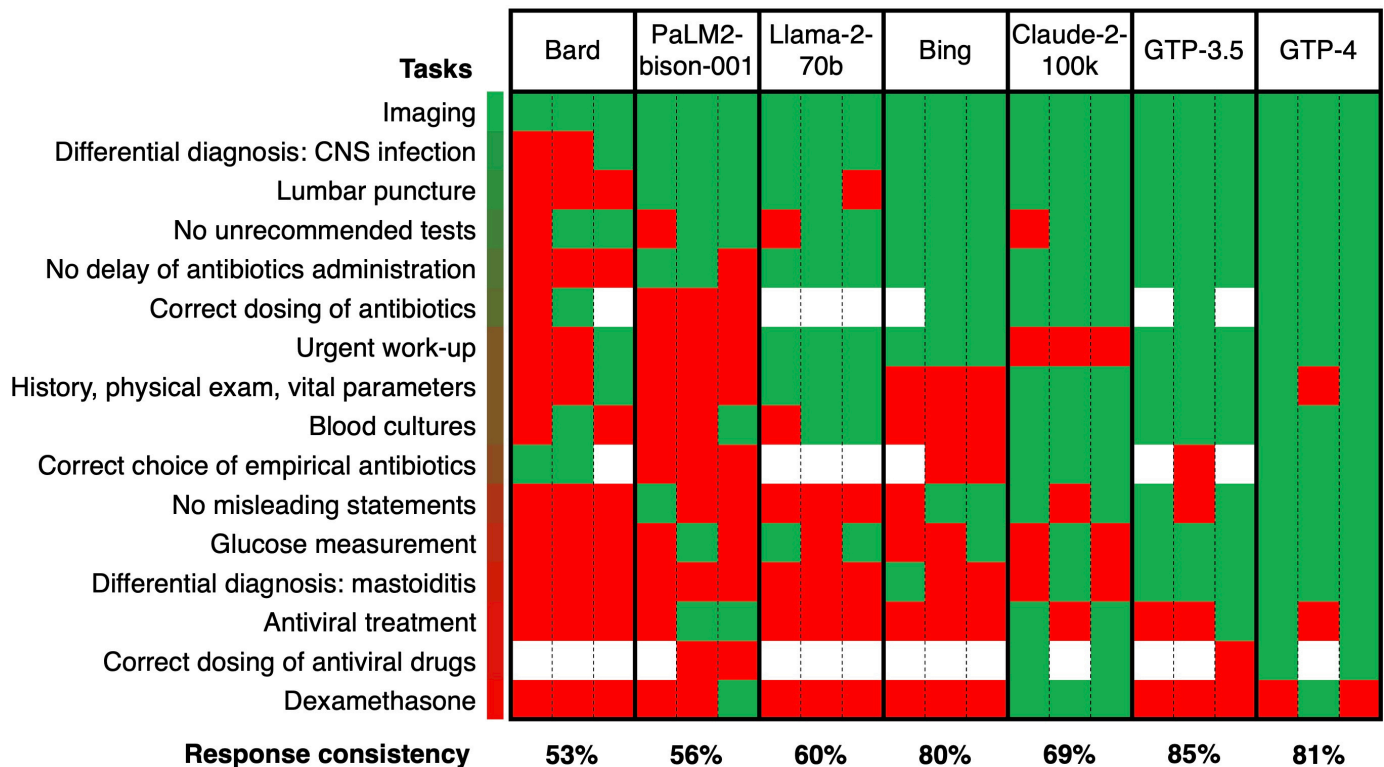


Figure 1 Qualitative assessment of large language models (LLMs) performance on a case of bacterial meningitis. Each LLM was tested three times with a standardised case vignette (individual sessions separated by dashed lines). Accomplished tasks are marked in green in decreasing order of agreement among all LLMs, while unaccomplished tasks are highlighted in red. White boxes represent tasks where the model either declined to respond or no additional information could be provided due to gaps in previous responses. Response consistency was defined as identically assessed responded tasks across different sessions of a single LLM. CNS, central nervous system.

the patient expresses any altered mental status and has downward drift of extremities, whereas according to the ESCMID guideline, a scan of the brain is not mandatory with a GCS>10) and maximal allowed delay to start antibiotics, these aspects were not included in the qualitative performance summary.^{14 16}

Statistics

Descriptive statistics with numbers and percentages and the two-sided Pearson correlation coefficient were used where appropriate (R, V.4.3.1). Due to the principally qualitative aim of this study, a statistical comparison between the LLMs was not intended.

RESULTS

The individual responses of all 21 sessions of the seven LLMs are summarised in figure 1. We noticed marked differences in the qualitative performance summary between different LLMs and to a lesser extent also between different sessions of individual LLMs. The response consistency ranged from 53% to 85%. LLMs with low numbers of accomplished tasks also had low response consistency. Among all the LLMs evaluated, GTP-4 demonstrated the most consistent performance, effectively addressing almost all tasks and having a high response consistency across all tasks and responses. Exemplary transcripts of

the first conversations with Bard and GTP-4 are shown in online supplemental material.

The word count of individual LLMs sessions varied significantly, ranging from 325 (PaLM 2 chat-bison-001) to 2045 (GTP-3.5), with an average of 1270 words (standard deviation 477). There was no significant correlation ($r=0.29$, $p=0.20$) between the total length of individual LLM responses and the summative performance of accomplished tasks, indicating that simply generating more text output does not necessarily lead to improved performance.

Suggested differential diagnoses and recommended diagnostic work-up

In 62% of the sessions, LLMs suggested an urgent work-up without direct prompting. In 57% of sessions, they recommended measuring vital parameters, taking the patient's history and performing a physical examination as initial steps. Furthermore, in 90% of the sessions, the LLMs accurately suspected a central nervous system (CNS) infection as a possible cause of the patient's symptoms. However, only 38% of the responses mentioned mastoiditis as a potential underlying cause or suggested correspondent diagnostic procedures (imaging with purpose of investigating mastoiditis, otoscopy, ear–nose–throat consultation). The most frequently mentioned differential diagnoses

were stroke (86%), followed by intracranial/subarachnoid haemorrhage and brain tumour (both 48%). Other proposed differential diagnoses were migraine (19%), metabolic/endocrine disbalances (19%), medication side effects (10%), non-CNS infections (10%), severe hypertension (5%), drug intoxication (5%) and neurodegenerative disorders (5%).

Regarding diagnostic work-up, cranial imaging was recommended in 100% of sessions, LP in 81% and blood cultures in 62%. Blood glucose measurement in the diabetic patient with altered mental status was suggested in 53%. Unrecommended tests by the IDSA and ESCMID guidelines (eg, electroencephalogram, electrocardiogram, chest radiography) were proposed in 19% of sessions as an initial work-up.

In 43% of responses, LLMs stated that a cranial CT scan is necessary before LP, while 14% suggested to perform an LP without CT scan and another 43% gave unclear answers. Only three LLMs (GTP-3.5, Claude-2, GTP-4) provided a case-specific rationale for their recommendation (92% responses suggested CT scan before LP). Due to different definitions of criteria for cranial imaging before LP in the reference guidelines and maximal allowed delay to start antibiotics,^{14 16} these aspects were not included in the qualitative performance summary displayed in [figure 1](#).

Recommended treatment

Regarding treatment, 81% of responses stated that rapid administration of antibiotics is necessary. The correct choice of empirical antibiotic treatment, consisting of a third-generation cephalosporin with ampicillin (alternatives: amoxicillin, penicillin G) with or without vancomycin, was provided in 38%, and of those, almost 90% with correct dosing.^{14 16} Another 29% provided an incomplete choice of antibiotic treatment and 33% declined to comment on any choice of antibiotics. In 33% of the sessions, antiviral treatment was considered with approximately half of them providing correct dosing. Dexamethasone administration was recommended in 24% of all responses.

Misleading statements

Misleading statements were identified in 52% of the sessions, such as performing an LP to relieve intracranial pressure or carrying it out prior to imaging in order to facilitate image interpretation; administering prophylactic antiseizure medication or giving benzodiazepines for sedation; adjusting ceftriaxone dosage based on age, weight and kidney function or administering dexamethasone for meningococcal meningitis; the presence of a stiff neck and Kernig's sign (while the vignette stated that these were absent); or the misinterpretation of mastoiditis as herpes zoster ophthalmicus.

DISCUSSION

This study investigated qualitative performance characteristics of different LLMs when challenged with a hypothetical clinical case of an adult patient with bacterial

meningitis and revealed marked discrepancies between the LLMs. This reflects both the potentials and limitations of these models when used as a guidance for medical work-up and treatment.⁹ The differences in qualitative performances observed among the LLMs did not demonstrate a correlation with the length of their respective outputs. This suggests that the performance variations can be attributed to the unique algorithmic designs of each LLM rather than their quantitative output.

CNS infection was identified as a probable cause among other differential diagnosis in the majority of cases and almost all LLMs succeeded in identifying and recommending appropriate investigations, including cranial imaging and LP. A fair proportion underscored the need for urgent diagnostics and antibiotic treatment. These results align with previous findings demonstrating a satisfactory performance of GTP-3 (the predecessor of GTP-3.5) in terms of triage and reasoning on differential diagnoses and the high performance of GTP-4 in diagnostic case challenges.^{4 19-21} Our study expands on these findings by examining an additional five LLMs which were not available at the time of the previous studies.

Our investigation also highlights limitations of most LLMs regarding their understanding of case complexity and their ability to link different disease entities. For instance, the identification of mastoiditis as an underlying cause was mentioned infrequently, as were blood glucose measurements, drawing blood cultures, considerations of empirical antiviral treatment and the administration of dexamethasone. The considerable heterogeneity in the responses of individual LLMs, despite standardised prompts, raises further concerns about their reliability and consistency. The presentation of misleading statements in more than half of the LLM sessions underscores the potential risk that comes along with their use for critical medical decision-making, especially in complex, life-threatening and time-sensitive situations, such as with bacterial meningitis. Such challenges must be addressed in future research when developing tools on the basis of LLMs for medical purposes.¹⁰⁻¹²

Most LLMs' inability to provide definitive guidance on whether to conduct a cranial CT scan before an LP might be due to the differences in the guidelines.^{14 16} However, the lack of clear direction in many LLM responses could also suggest an insufficiency in handling complex clinical situations where there is a need for reasoned decision-making. This finding may be viewed in the context of the research gap between healthcare AI development and the challenge of its validation and implementation in real-world clinical settings.²²⁻²⁴

Limitations

Our study has several limitations. Most importantly, none of the LLMs was designed to assist in medical diagnostics and treatment and most correctly included respective disclaimers. However, as LLMs are powerful, new and easily accessible AI tools, it is highly probable that they will find increasing use in the health sector, which

justifies studying their reliability and applicability.¹⁻⁶ Further, prompting has significant influence on the result.¹³ While our study did not explore the impact of different prompting strategies, we used standardised prompts, which included contextualisation and step-by-step reasoning, to ensure comparability between LLMs. Although we evaluated the LLMs' intuitive assessment of the scenario's urgency, we did not directly inquire this in the prompts. In addition, the selection of tasks for the qualitative assessment was unweighted and focused on important initial management steps, while other aspects, such as laboratory testing procedures or duration of antimicrobial treatment, were not investigated. Lastly, the study was limited to a single case scenario, and the results may not be generalisable to other clinical scenarios. Thus, we refrained from an absolute ranking of the LLMs.

CONCLUSIONS

The latest versions of LLMs show potential in helping healthcare professionals. Our study underscores the need for cautious and informed use of most of these models as demonstrated by the limitations in providing specific information and potentially misleading information for diagnostic work-up and treatment of adult patients with bacterial meningitis. Users should be aware of the variability in their performance.

Further research is needed to refine these models and enhance their understanding of complex medical scenarios and their ability to provide deterministic, reliable information regardless of prompt nuances. Concurrently, efforts are necessary to mitigate the potential for disseminating erroneous content.

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Content:

S-1 Supplemental Table 1: Standardized prompts for individual sessions with the LLMs.

S-2 Supplemental Table 2: Definition of qualitative assessment of tasks reflecting good clinical practice and adherence to reference meningitis guidelines.

S-5 Supplemental Text: Full transcript of the first conversation with Bard and GTP-4.

Supplemental Table 1: Standardized prompts for individual sessions with the LLMs.

Acronyms: CT = computed tomography; LLM = large language model.

Prompt	Content	Commentary
1	You are an experienced medical assistant who gives the most accurate answers based on your knowledge. I am a junior medical doctor seeking your medical advice. A 52-year-old female patient presents with severe headache and confusion. > What are the next steps?	Asked in each session.
2	History: Her friend found her at her home 2 hours ago in a confused state and brought her to the hospital. She was last seen well yesterday. The patient is disoriented but states that she has severe headache and wishes to be alone. Further history taking is not possible due to her confused state. Her friend says she has type 2 diabetes, arterial hypertension and migraine with aura. Physical examination: She appears lethargic. She opens her eyes to pain only. She is disoriented to date, place and the current situation. She can only follow simple commands. All extremities have a fast downward drift when held in the air. She has a rhythmic pulse of 120/minute and a respiratory rate of 20/min with peripheral O ₂ saturation of 95%. Her blood pressure is 125/85 mmHg and her temperature is 38.7 °C. Upon auscultation, her heart and lungs are clear. Bowel sounds are normal. Her abdomen is soft and non-tender, with no flank pain. Her neck is not stiff. She has a tender red spot behind her right ear. > Provide me with a detailed step-wise recommendation how to proceed.	Asked in each session. Additional details of physical examination were provided only if the LLM specifically requested for it. These were: pupil status (response: normal examination), coordination testing (response: dysmetria), gait (response: testing not feasible).
3	> Do I have to wait for a CT scan of the head before performing the lumbar puncture? > Do I have to wait to administer antibiotics until I have done the lumbar puncture?	Asked in each session.
4	> Provide me with the exact dosages of antibiotics.	Asked in each session.
5	> Is there anything else I need to consider regarding the treatment or workup of this patient?	Asked in each session.

Supplemental Table 2: Definition of qualitative assessment of tasks reflecting good clinical practice and adherence to reference meningitis guidelines.

Acronyms: CNS = central nervous system; CT = computed tomography, ENT = Ear, nose and throat; ESCMID = European Society of Clinical Microbiology and Infectious Diseases; IDSA = Infectious Diseases Society of America; LLM = large language model; LP = Lumbar puncture; MRI = magnetic resonance imaging.

* These tasks were not considered for the performance assessment due to different definitions by the reference guidelines.

Task	Definition of Accomplishment	Background / Details
Urgent work-up	The LLM provides substantial commentary on expedited diagnostic procedures by terms such as "urgent", "STAT", "rapid", "immediate", etc. to denote the immediacy and speed of these processes.	Delay in the initiation of therapy in bacterial meningitis patients is strongly associated with death and poor outcome ^{11,13} .
History, physical exam, vital parameters	Medical history of the current problem, physical examination and measuring vital parameters (pulse, blood pressure, respiratory rate) is suggested by the LLM after prompt 1.	Clinical evaluation of patients with acute symptoms should consist of obtaining the medical history, a physical examination and vital parameters.
Glucose measurement	Glucose measurement is suggested by the LLM.	In patients with acutely altered mental status, especially those with known diabetes mellitus, a derangement of glucose metabolism should be rapidly excluded.
Blood cultures	Obtaining blood samples for microbiological culture is suggested by the LLM after prompt 1 or 2.	If there is suspicion of acute bacterial meningitis, blood cultures must be obtained immediately ¹³ , before the first dose of antibiotics is administered ¹¹ .
Imaging	Cranial CT or MRI is suggested by the LLM as a response to prompt 1 or prompt 2.	The differential diagnosis for acutely altered mental status is broad and includes other acute brain disorders beside CNS infection, such as stroke or subarachnoid hemorrhage. Cranial imaging is indicated in such a situation. Further, cerebral imaging can demonstrate complications of CNS infection such as edema or hydrocephalus, which require additional therapeutic measures ¹² .
LP	LP is suggested by the LLM as a response to prompt 1 or 2.	In patients with suspected bacterial meningitis, it is strongly recommended to determine CSF leukocyte count, protein and glucose concentration, and to perform CSF culture and Gram stain ^{11,13} .
No unrecommended tests	Any initial diagnostic test suggested by the LLM after prompt 1 or 2 which is not reflected by the reference guidelines for the given scenario ^{11,13} .	A summary of the suggested diagnostic tests is provided in Table 3 of the systematic review by Sigfrid et al. (2019) ¹⁴ .

No misleading statements	Either erroneous conclusions by the LLM of specific information or wrongful statements which contradict general knowledge or recommendations by the reference guidelines ^{11,13} .	
Differential diagnosis: CNS infection	Clear statement indicating infection of the CNS, such as "Meningitis", "Encephalitis", "Meningoencephalitis", or "Brain abscess" by the LLM as a response to prompt 1 or prompt 2.	In adults, the most common clinical characteristics of bacterial meningitis are fever, headache, neck stiffness and altered mental status. However, these can be absent and therefore bacterial meningitis should not be ruled out solely on the absence of such typical symptoms ¹¹ .
Differential diagnosis: mastoiditis	LLM includes mastoiditis in its differential diagnoses and/or suggests specific work-up (imaging with purpose of investigating mastoiditis, otoscopy, ear nose throat consultation, etc).	A search for an infectious focus is crucial and patients should be examined for otitis media or mastoiditis ¹² . Cranial imaging for other diagnostic purposes such as the detection of mastoiditis or sinusitis should be performed. ¹¹ 30/12/2023 14:16:00
Correct choice of empirical antibiotics	The LLM provide assertively a correct choice of empirical antibiotic treatment when specifically asked. For a patient >50 years with diabetes mellitus, an initial empirical antibiotic treatment should cover for <i>Listeria monocytogenes</i> .	According to ESCMID ¹¹ : Ceftriaxone or cefotaxime, amoxicillin or ampicillin or Penicillin G, optionally vancomycin or rifampicin if reduced <i>Streptococcus pneumoniae</i> antimicrobial sensitivity is suspected: vancomycin 20–60 mg/kg/day or rifampicin 600mg/d. According to IDSA ¹³ : ceftriaxone or cefotaxime, ampicillin, vancomycin.
Correct dosing of antibiotics	Correct dosing of empirical antibiotic treatment is suggested by the LLM as a response to prompt 4 for an adult patient >50 years with diabetes mellitus.	According to ESCMID ¹¹ : Ceftriaxone 4g/day or cefotaxime 8-12g/day, amoxicillin or ampicillin 12g/day or Penicillin G. If reduced <i>Streptococcus pneumoniae</i> antimicrobial sensitivity: vancomycin 20–60 mg/kg/day or rifampicin 600mg/d. According to IDSA ¹³ : ceftriaxone 4g/day or cefotaxime 8-12g/day, ampicillin 12g/day, vancomycin 30–45 mg/kg/day.
No delay of antibiotics administration	Statement by the LLM that antibiotics should be administered promptly without unnecessary delay.	Strong recommendation to start antibiotic therapy as soon as possible. The time period until antibiotics are administered should be less than 1 hour ¹¹ . Whenever lumbar puncture is delayed, e.g. due to cranial imaging, empiric treatment must be started immediately on clinical suspicion, even if the diagnosis has not been established ^{11,13} .
Antiviral treatment	Antiviral treatment is suggested by the LLM to be considered as a conjunctive to antibacterial treatment.	The clinical findings of bacterial meningitis overlap with those of meningitis caused by viruses. Clinical judgement is key when considering whether to start empiric antibiotic and adjunctive therapy ¹¹ . The diagnosis of viral encephalitis is suspected in the context of a febrile disease accompanied by headache, altered level of consciousness and signs of cerebral dysfunction. Treatment with acyclovir should be commenced on clinical suspicion ¹⁵ .
Correct dosing of antiviral drugs	If antiviral treatment is suggested by the LLM, the LLM states the correct dose.	Acyclovir 10mg/kg three times a day ¹⁵ .

Dexamethasone	Dexamethasone is suggested by the LLM as a conjunctive to anti-infective treatment.	<p>Empiric treatment with dexamethasone is strongly recommended for all adults with acute bacterial meningitis in the setting of high-income countries with the first dose of antibiotic treatment¹¹.</p> <p>In adults with suspected or proven pneumococcal meningitis, dexamethasone should be administered before or concomitant with the first dose of antimicrobial therapy¹³.</p>
Cranial imaging before LP *	Clear statement by the LLM as a response to prompt 3 whether cranial imaging should be performed before the LP or not.	<p>Indication for cranial imaging before LP according to ESCMID¹¹: Strong recommendation only if focal neurologic deficits (excluding cranial nerve palsies), new-onset seizure, severely altered mental status (GCS <10), severely immunocompromised state. In patients lacking these characteristics, cranial imaging before lumbar puncture is not recommended.</p>
Case-specific explanation for decision regarding cranial imaging before LP *	The LLM provides a comprehensible case-specific explanation for its decision regarding the necessity for cranial imaging before LP which reflects recommendations by the reference guidelines ^{11,13} .	<p>Indication for cranial imaging before LP according to IDSA¹³: immunocompromised state, history of CNS disease, new onset seizure, papilledema, abnormal level of consciousness, focal neurologic deficit (including dilated nonreactive pupil, abnormalities of ocular motility, abnormal visual fields, gaze palsy, arm or leg drift). Strong recommendation to start antibiotic therapy as soon as possible. The time period until antibiotics are administered should be less than 1 hour¹¹. Whenever lumbar puncture is delayed, e.g. due to cranial imaging, empiric treatment must be started immediately on clinical suspicion, even if the diagnosis has not been established^{11,13}.</p>
Antibiotic treatment before LP *	The LLM suggests antibiotic treatment before the LP if it recommended to perform a CT scan prior.	<p>Antibiotic treatment in patients with acute bacterial meningitis should be started as soon as possible, and the time period from entering the hospital to initiation of antibiotic treatment should not exceed 1 hour¹¹. Whenever lumbar puncture is delayed, e.g., due to cranial CT, empiric treatment should be started upon clinical suspicion beforehand after obtaining blood cultures^{11,13}.</p>

Supplemental Text: Full transcript of the first conversation with Bard and GTP-4 (user prompts in bold).Bard

You are an experienced medical assistant who gives the most accurate answers based on your knowledge. I am a junior medical doctor seeking your medical advice. A 52-year-old female patient presents to the hospital with severe headache and confusion.
> What are the next steps?

Hi there, junior medical doctor.

The next steps for a 52-year-old female patient who presents to the hospital with severe headache and confusion include:

- 1 A complete history and physical examination. This will help to determine the cause of the headache and confusion, as well as any other underlying medical conditions.
- 2 Laboratory tests. These may include a complete blood count, blood chemistry, urinalysis, and imaging studies such as a CT scan or MRI of the brain.
- 3 Treatment. The treatment for a severe headache and confusion will depend on the underlying cause. However, in some cases, treatment may include medication to relieve pain, anti-convulsants to prevent seizures, or antibiotics to treat an infection.

It is important to note that the next steps for a patient with severe headache and confusion may vary depending on the individual patient's symptoms and medical history. However, the steps outlined above are a good starting point for any patient who presents with these symptoms.

Here are some additional things to keep in mind:

- The patient should be monitored closely for changes in their condition.
- The patient should be treated for any underlying medical conditions that are found.
- The patient should be educated about the signs and symptoms of a stroke or other serious medical emergencies.

I hope this helps!

History: Her friend found her at her home 2 hours ago in a confused state and brought her to the hospital. She was last seen well yesterday. The patient is disoriented but states that she has severe headache and wishes to be alone. Further history taking is not possible due to her confused state. Her friend says she has type 2 diabetes, arterial hypertension and migraine with aura. Physical examination: She appears lethargic. She opens her eyes to pain only. She is disoriented to date, place and the current situation. She can only follow simple commands. All extremities have a fast downward drift when held in the air. She has a rhythmic pulse of 120/minute and a respiratory rate of 20/min with peripheral O₂ saturation of 95%. Her blood pressure is 125/85 mmHg and her temperature is 38.7 °C. Upon auscultation, her heart and lungs are clear. Bowel sounds are normal. Her abdomen is soft and non-tender, with no flank pain. Her neck is not stiff. She has a tender red spot behind her right ear.
> Provide me with a detailed step-wise recommendation how to proceed.

Sure, here is a detailed step-wise recommendation on how to proceed with this patient:

- 1 Complete a full neurological examination. This will assess the patient's level of consciousness, orientation, and motor function. It is important to note that the patient's mental status may be altered due to her headache and confusion, so it is important to be as objective as possible in your assessment.
- 2 Order a complete blood count, blood chemistry, urinalysis, and chest X-ray. These tests will help to rule out any underlying medical conditions that could be causing the patient's symptoms.
- 3 Order a CT scan or MRI of the brain. These imaging studies will help to visualize the brain and look for any signs of stroke, tumor, or other structural abnormalities.
- 4 Start the patient on IV fluids and anti-convulsants. This will help to prevent seizures and keep the patient hydrated.
- 5 Monitor the patient closely for changes in their condition. This includes monitoring their vital signs, neurological status, and fluid balance.

If the patient's condition does not improve with treatment, or if they develop any new symptoms, you may need to consider other diagnostic tests or treatment options.

Here are some additional things to keep in mind:

- The patient's friend should be interviewed to get more information about the patient's medical history and the events leading up to her presentation to the hospital.
- The patient's family should be informed about her condition and the plan of care.
- The patient should be educated about the signs and symptoms of a stroke or other serious medical emergencies.

I hope this helps!

- > **Do I have to wait for a CT scan of the head before performing the lumbar puncture?**
- > **Do I have to wait to administer antibiotics until I have done the lumbar puncture?**

The decision of whether or not to wait for a CT scan of the head before performing a lumbar puncture is a complex one that depends on a number of factors, including the patient's clinical presentation, the results of their initial laboratory tests, and the availability of imaging resources.

In general, if the patient has a clear indication for a lumbar puncture, such as a suspected meningitis or encephalitis, then the lumbar puncture should be performed as soon as possible. This is because a delay in diagnosis and treatment can have serious consequences, such as permanent neurological damage or death. However, if the patient's clinical presentation is less clear, or if the availability of imaging resources is limited, then it may be prudent to wait for a CT scan of the head before performing a lumbar puncture. This is because a CT scan can help to rule out other conditions that can mimic meningitis or encephalitis, such as a subarachnoid hemorrhage or a brain tumor.

The decision of whether or not to wait to administer antibiotics until after the lumbar puncture is also a complex one. In general, if the patient has a high clinical suspicion for meningitis or encephalitis, then antibiotics should be started as soon as possible. This is because the delay in treatment can have serious consequences, such as permanent neurological damage or death.

However, if the patient's clinical presentation is less clear, or if there is a concern about the possibility of a subarachnoid hemorrhage, then it may be prudent to wait for the results of the lumbar puncture before starting antibiotics. This is because antibiotics can obscure the results of the lumbar puncture, making it difficult to diagnose meningitis or encephalitis.

Ultimately, the decision of whether or not to wait for a CT scan of the head before performing a lumbar puncture, or whether or not to wait to administer antibiotics until after the lumbar puncture, is a clinical one that should be made on a case-by-case basis.

Here are some additional factors to consider when making these decisions:

- The patient's age and overall health status.
- The patient's clinical presentation.
- The results of the patient's initial laboratory tests.
- The availability of imaging resources.
- The patient's wishes.

It is important to consult with a qualified healthcare professional to make the best decision for each individual patient.

> **Provide me with the exact dosages of antibiotics**

The exact dosages of antibiotics for meningitis will vary depending on the patient's age, weight, and other medical conditions. However, the following are some general guidelines:

- Ceftriaxone: 1 g IV every 24 hours for adults and children over 12 years old.
- Cefotaxime: 2 g IV every 8 hours for adults and children over 12 years old.
- Ampicillin: 2 g IV every 4 hours for adults and children over 12 years old.
- Penicillin G: 20 million units IV every 4 hours for adults and children over 12 years old.

It is important to note that these are just general guidelines, and the specific dosages of antibiotics will need to be determined by a qualified healthcare professional.

Here are some additional things to keep in mind:

- Antibiotics should be started as soon as possible after diagnosis.
- Antibiotics should be continued for at least 7 days, or longer if the patient is not responding to treatment.
- Patients should be monitored closely for side effects of antibiotics, such as rashes, diarrhea, and nausea.

I hope this helps!

> **Is there anything else I need to consider regarding the treatment or workup of this patient?**

Yes, there are a few other things to consider regarding the treatment or workup of this patient:

- The patient's age and overall health status. Meningitis can be more serious in young children and older adults, so it is important to consider their age and overall health status when making treatment decisions.
- The patient's clinical presentation. The patient's clinical presentation can provide clues about the underlying cause of their meningitis. For example, patients with meningococcal meningitis often have a more rapid and severe course of illness than patients with pneumococcal meningitis.
- The results of the patient's laboratory tests. The results of the patient's laboratory tests can help to confirm the diagnosis of meningitis and identify the organism responsible for the infection.

- The availability of imaging resources. Imaging resources, such as a CT scan or MRI of the brain, can help to rule out other conditions that can mimic meningitis, such as a subarachnoid hemorrhage or a brain tumor.
 - The patient's wishes. It is important to discuss the patient's wishes for treatment with them and their family. This includes discussing the risks and benefits of different treatment options, as well as the patient's goals of care.
- I hope this helps!

GTP-4

> You are an experienced medical assistant who gives the most accurate answers based on your knowledge. I am a junior medical doctor seeking your medical advice. A 52-year-old female patient presents to the hospital with severe headache and confusion. What are the next steps?

The symptoms presented by this patient - severe headache and confusion - could be caused by a range of conditions. These might be as varied as migraines, meningitis, encephalitis, a stroke, a brain tumor, or other neurological conditions. As a junior medical doctor, you should follow a systematic approach to evaluate the patient. Here's a suggested approach:

- 1 **Immediate Stabilization** If the patient appears acutely ill, ensure her vital signs are stable (blood pressure, heart rate, respiration rate, oxygen saturation, temperature). If she is unstable, follow the hospital's emergency protocol.
- 2 **Detailed History** Get a detailed history. Try to identify when the headache started, any accompanying symptoms, if there was any triggering event, any similar past history, any medication she is currently on, and any chronic illnesses.
- 3 **Physical Examination** Perform a thorough physical examination including a detailed neurological examination. This should include testing cranial nerves, motor and sensory function, reflexes, coordination and gait. Also look for signs of infection (like neck stiffness, fever), trauma, and other systemic illnesses.
- 4 **Differential Diagnosis** Based on the history and physical examination, list your differential diagnoses. These might include but are not limited to: migraine, tension headache, cluster headache, brain tumor, stroke, meningitis, encephalitis, or brain abscess.
- 5 **Laboratory and Imaging Studies** You might need to order some lab tests and imaging studies depending on your differential diagnoses. Commonly used tests could be CBC, blood culture, liver function test, coagulation profile, CT or MRI of the brain. If an infection like meningitis is suspected, a lumbar puncture might be needed.
- 6 **Consultation** Depending on the suspected diagnoses, you might need to consult with specialists like a neurologist or infectious disease specialist.
- 7 **Treatment** Start treatment based on your most likely diagnosis. For instance, if a stroke is suspected, the patient needs immediate intervention. If an infection is suspected, start empirical antibiotics while waiting for culture report.

This is a general outline and the actual steps might vary depending on the patient's condition and the hospital's protocol. You should always discuss with your seniors or specialists whenever in doubt. Remember that severe headache with confusion is potentially serious and needs to be evaluated urgently.

History: Her friend found her at her home 2 hours ago in a confused state and brought her to the hospital. She was last seen well yesterday. The patient is disoriented but states that she has severe headache and wishes to be alone. Further history taking is not possible due to her confused state. Her friend says she has type 2 diabetes, arterial hypertension and migraine with aura.

Physical examination: She appears lethargic. She opens her eyes to pain only. She is disoriented to date, place and the current situation. She can only follow simple commands. All extremities have a fast downward drift when held in the air. She has a rhythmic pulse of 120/minute and a respiratory rate of 20/min with peripheral O₂ saturation of 95%. Her blood pressure is 125/85 mmHg and her temperature is 38.7 °C. Upon auscultation, her heart and lungs are clear. Bowel sounds are normal. Her abdomen is soft and non-tender, with no flank pain. Her neck is not stiff. She has a tender red spot behind her right ear. Cranial nerves and reflexes and sensory function to touch are normal. Coordination tests show dysmetria. Gait testing is not possible due to her condition. There are no signs of trauma or other systemic illnesses.

> Provide me with a detailed step-wise recommendation how to proceed.

Based on the history and physical examination, your patient is showing signs of altered mental status with confusion and lethargy, indicating potential encephalopathy. The fever suggests a possible infection. The tender

red spot behind her ear might indicate an infection such as mastoiditis, which could potentially lead to a brain abscess or meningitis. The dysmetria and drift in all extremities suggest a central nervous system involvement. Here's a step-by-step approach on how to proceed:

1 **Immediate Stabilization** The patient's vital signs are relatively stable, but she needs to be monitored closely due to her confused state and fever. Ensure she is safe and comfortable. Administer oxygen if necessary (if SpO₂ falls <94%).

2 **Laboratory Tests** Order the following:

- CBC: To check for infection or other hematological conditions.
- Blood Culture: If bacteremia is suspected.
- Blood Glucose: Given the history of diabetes.
- Liver and Renal Function Tests: To evaluate metabolic causes of encephalopathy.
- Coagulation Profile: As she could be a candidate for lumbar puncture.
- CRP/ESR: These markers can help identify an ongoing inflammation or infection.
- Urinalysis: To rule out urinary tract infection, which can cause confusion in older patients.

3 **Imaging Studies**

- CT Head: Urgently needed to rule out stroke, brain abscess, or other structural brain diseases. Given the history of arterial hypertension, it's important to rule out intracerebral hemorrhage.
- CT/MRI Temporal Bone: If mastoiditis is suspected from the tender red spot behind the ear.

4 **Lumbar Puncture** If imaging does not reveal a contraindication (like raised intracranial pressure), perform a lumbar puncture to rule out meningitis, encephalitis, or other CNS infections.

5 **Treatment**

- Start empirical antibiotics after taking appropriate cultures, given the fever and possible infection source from the red spot behind the ear.
- Treat other abnormalities found in lab results.

6 **Consultation**

- Consult Neurology: Given the altered mental status and neurological findings.
- Consult Infectious Disease: If the infection is confirmed or highly suspected.
- Consult ENT: If mastoiditis is suspected.

7 **Monitoring**

- Monitor her vital signs, mental status, and neurological function closely.
- Regularly reassess the patient and adjust the treatment based on lab and imaging results and consultation inputs.

This is a serious situation, and the patient needs to be evaluated and managed urgently. It's important to communicate and coordinate with your team and the consulting specialists, and to keep the patient's family or friend informed in a sensitive and appropriate manner.

> Do I have to wait for a CT scan of the head before performing the lumbar puncture? > Do I have to wait to administer antibiotics until I have done the lumbar puncture?

1 **CT Scan Before Lumbar Puncture:** In general, it is recommended to perform a CT scan before a lumbar puncture if there are signs that suggest the patient may have elevated intracranial pressure, focal neurological deficits, papilledema, altered level of consciousness, or if the patient is immunocompromised. The concern is that a lumbar puncture in the presence of increased intracranial pressure could potentially lead to brain herniation, a life-threatening condition. In this patient, given the altered mental status and neurological findings, it would be prudent to perform a CT scan of the head before a lumbar puncture.

2 **Administering Antibiotics Before Lumbar Puncture:** If bacterial meningitis is suspected, it is recommended to start antibiotics as soon as possible, even before lumbar puncture is performed, if it's going to be delayed. Rapid administration of antibiotics can be life-saving. However, it's important to collect blood cultures before starting antibiotics if possible. In this patient, given the fever and potential source of infection, starting empirical antibiotics after taking appropriate cultures would be a reasonable decision. If a lumbar puncture cannot be performed immediately (for example, if waiting for the CT scan results), this should not delay the initiation of antibiotics.

Remember, these decisions should be made in collaboration with the wider healthcare team, including senior doctors and consulting specialists, and should take into account the specific condition and stability of the patient.

> Provide me with the exact dosages of antibiotics

The choice of antibiotic and the dose will depend on the suspected organism and the patient's weight, renal function, and allergies. Given that this patient may have a central nervous system infection and possibly a concurrent ear infection (mastoiditis), broad-spectrum coverage is needed.

Here is a typical regimen:

- 1 Ceftriaxone: 2g IV every 12 hours. This is a third-generation cephalosporin that covers a wide range of organisms including *Streptococcus pneumoniae* and *Neisseria meningitidis*, common causes of bacterial meningitis in adults.
- 2 Vancomycin: 15-20 mg/kg IV every 8-12 hours (not to exceed 2g/dose). This provides coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) and *Streptococcus pneumoniae* resistant to cephalosporins.
- 3 Amoxicillin: 2g IV every 4 hours. This is added to cover *Listeria monocytogenes*, which could be a consideration given the patient's age.
- 4 Acyclovir: 10 mg/kg IV every 8 hours. This is added to cover for possible herpes encephalitis, until it can be ruled out.

Please note: This is a broad and general antibiotic regimen for serious CNS infections. The exact choice of antibiotics and dosages should be tailored to the patient's individual needs (including considerations such as allergies and renal function) and local antibiotic resistance patterns. The regimen should be adjusted based on culture results and consultation with Infectious Disease specialists.

In addition, due to the patient's confusion and lethargy, it's important to assess her swallowing reflex before administering oral medications. If her swallowing function is compromised, she might require a nasogastric tube for medication administration and nutrition, or the medications may need to be administered intravenously. Also, don't forget to provide supportive care like antipyretics for fever and analgesics for headache. Monitor all vital signs and glucose levels closely, especially considering the patient's history of diabetes.

> Is there anything else I need to consider regarding the treatment or workup of this patient?

Aside from the points previously mentioned, here are a few additional considerations:

- 1 Neurology Consultation: If not already done, a consultation with a neurologist would be beneficial. They can provide further insight into the neurological findings and help guide the management of the patient's condition.
- 2 Infectious Disease Consultation: Specialists in infectious disease can provide valuable input on antibiotic choice and duration of therapy, particularly if the patient doesn't respond to initial empiric therapy or if rare pathogens are suspected.
- 3 Monitoring Glucose Levels: Given the patient's history of diabetes, it is essential to monitor her blood glucose levels regularly. The stress of illness can cause significant fluctuation in glucose levels, and both hyperglycemia and hypoglycemia can worsen her confusion.
- 4 Review Medications: Review all current medications the patient is on. Certain drugs might contribute to her confusion, or interact with the treatments you are planning to give.
- 5 Nutrition and Hydration: Ensure the patient's nutritional needs are met. This can be challenging if she is lethargic and potentially unable to swallow. Consider the need for a nasogastric tube for feeding if necessary. Hydration is also important, particularly as fever can increase insensible water loss.
- 6 Follow-Up Imaging and Labs: Depending on the findings of the initial CT scan and laboratory tests, follow-up imaging or additional laboratory tests may be needed.
- 7 Reassessment: The patient should be reassessed regularly. If she doesn't improve or if she worsens on the current management plan, reassessment of the diagnosis and treatment plan will be necessary.
- 8 Communication: Keep open communication with the patient's family members or friends to update them about the patient's condition, while respecting patient confidentiality.
- 9 Documentation: Be sure to document all findings, decisions, and communication in the patient's medical record.

It's important to remember that each patient is unique, and while these are general steps and considerations, the exact approach should be tailored to the individual patient's condition and response to treatment.