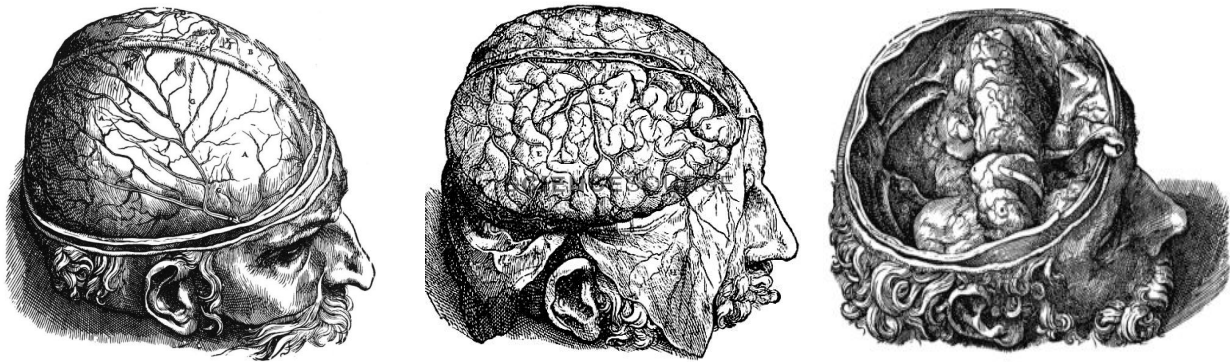


Microbiology

435's Teamwork
Neuropsychiatry Block



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- Kindly check our [Editing File](#) before studying the document.
 - Please contact the team leaders for any suggestion, question or correction.
 - Pay attention to the statements highlighted in **red**.
 - Extra explanations are added for your understanding in **grey**.
 - **Footnotes color code:** General | **Females** | **Males**

Revised by

خولة العماري & هشام الغنيلي



Chronic Cerebral and Meningitic Infections

Resources: Sherris Medical Microbiology, LIR Microbiology, Prof. Fawziya's & Dr. Somily's 2017 lectures.

Learning Objectives:

By the end of this lecture, you should know the...

1. Etiology
2. Identification
3. Clinical presentation
4. Diagnostic approaches
5. Treatment

Of chronic cerebral and meningitic infections.

Before going into details, we first are required to acknowledge that Tuberculosis and Brucellosis are the greatest concerns regarding chronic cerebral and meningitic infections in the region, therefore, although we will discuss almost all possible pathogens, our focal point must be favoring TB and Brucella in particular. Also, we advise you to study **Lecture (3): Acute Pyogenic Meningitis** first.

Clinical Presentation [Persistent, prolonged, and recurrent]

- Chronic CNS infections cause neurological disability and, may be fatal if untreated.
- They usually are slow, insidious in onset with progression of signs and symptoms over a period of weeks.
- They differ from those of acute infection by having a rapid onset of symptoms and signs and diagnosed for usually > 4 weeks if the neurological syndrome exists.
- Cerebral abscesses can be preferred as a chronic CNS infection.

Symptoms

- **Chronic headache.**
- Neck or back pain.
- Change in personality.
- **Facial weakness.**
- Double vision / Visual loss.
- Arm and leg weakness.
- Clumsiness.¹

Signs

- +/- Papilloedema.²
- Brudzinski³ or Kerning⁴ positive sign of meningeal irritation.
- Altered mental status (e.g. memory loss).
- 3rd, 4th, 6th and 7th cranial nerve palsy.
- Ataxia.
- Hydrocephalus.⁵

¹ Awkward in movement or action; without skill or grace: "He is very clumsy, he always break things."

² Optic disc swelling that is caused by increased intracranial pressure ([MORE](#)).

³ [VIDEO](#).

⁴ [VIDEO](#).

⁵ Abnormal accumulation of cerebrospinal fluid (CSF) within the brain.

Etiology		
Bacterial (Most Important)		
Partially Treated Acute Meningitis	In Saudi Arabia	Others ⁶
<i>Neisseria Meningitidis</i> <i>Streptococcus Pneumoniae</i> <i>Haemophilus influenzae</i>	<i>Brucella</i> ⁷ - Brucellosis <i>TB</i> ⁸ - Tuberculosis	<i>Treponema Pallidum</i> - Syphilis ⁹ <i>L. Ictero haemorrhagica</i> - Leptospirosis ¹⁰ <i>Borrelia burgdorferi</i> - Lyme Disease ¹¹ <i>Nocardia Asteroids</i> - Nocardiosis ¹²
Fungal		Parasitic
In Saudi Arabia	Others	Viral
<i>Candida Albicans</i> ¹⁷	<i>Cryptococcus Neoformans</i> ¹⁸ <i>Histoplasma Capsulatum</i> <i>Aspergillus Species</i> ¹⁹	<i>Toxoplasma Gondii</i> ¹³ <i>Trypanosoma Brucei</i> ¹⁴ <i>Acanthamoeba Species</i> ¹⁵
		<i>Mumps Virus</i> <i>Herpes Simplex Virus (HSV)</i> <i>Human Immunodeficiency Virus (HIV)</i> ¹⁶ <i>Cytomegalovirus (CMV)</i>

⁶ They are not common in KSA so you can think of them but they would be at the bottom of the list.

⁷ Brucella Cannot be diagnosed with CSF, we conduct a Serology test to look for Brucella. In case of severe infection in the CNS you have to think about Brucella.

⁸ Chronic infection (fever for multiple weeks, losing weight), if the patient was in KSA we automatically think of TB.

TB meningitis usually happens at the base of the skull, so it is very difficult to take a biopsy, we ask for an **AP smear**, PCR, TB Culture to diagnose.

TB & Brucella are common & they can cause any infection including CNS.

⁹ Chronic bacterial disease that is contracted chiefly by infection during sexual intercourse.

¹⁰ **Very rare.** Bacterial disease that occurs in rodents, dogs, and other mammals and can be transmitted to humans. It is common in India, South America.

¹¹ Not common in Saudi Arabia. Transmitted to humans through the bite of infected blacklegged ticks.

¹² Infectious disease affecting either the lungs (pulmonary) or the whole body (systemic). **They are present in the environment.** It is a systemic disease that affects immunosuppressed patients (such as post transplant patients, patients on steroid and autoimmune patients on cortisone). It is acquired through inhalation and will pass through the bloodstream to cause a brain abscess.

¹³ AIDs defining disease.

¹⁴ T. Gambiense in particular + it causes Trypanosomiasis. Case could be that the patient went to Africa and was bitten.

¹⁵ Causes eye infections and CNS infections in people who have a sort of immunosuppression.

¹⁶ May present with meningitis either due to the virus itself or due to a superimposed infection.

¹⁷ **Always associated with diabetics and immunocompromised patients.** It's related to nosocomial interventions or surgeries.

¹⁸ AIDs defining disease. It is a capsulated organism, identified in the CSF using the India ink to show the very characteristic capsule. It's difficult to treat.

¹⁹ Can affect anybody but particularly related to immunosuppression.

Diagnosis:

- **For syphilis:** VDRL and other serological causes.
- **For fungal and parasite:** Wet preparation of CSF.
- **For *Cryptococcus neoformans*:** India ink.
- **For *Brucella*, *TB*, *Leptospira* other Bacteria:** Culture CSF.

Findings of CSF analysis				
Normal				Chronic Cerebral and Meningitic Infection
Adults	Neonates			
	Term	Preterm		
WBC	0-5 / cm^3	0-32 / cm^3	0-29 / cm^3	
PMN²⁰	0%	> 60%	> 60%	Insignificant ²¹
Protein	< 30 mg/dl	20-170 mg/dl	60-150 mg/dl	Increased ²²
Glucose	> 60%	> 60%	> 60%	Reduced

Brucellosis ²³	
Etiology	Brucella Species Gram -ve Coccobacilli <i>Brucella Melitensis</i> ²⁴ is the most common in Saudi Arabia
Transmission	Contact with domestic animals ²⁵ or consumption of raw milk and dairy products
Presentation	<ul style="list-style-type: none"> • It usually presents with Pyrexia (fever) of unknown organism of intermittent nature. • The fever is accompanied by night sweating, however, in between the attacks of fever the patient is not very ill. • Because the symptoms are not specific and flu-like, untreated Brucella can invade the CNS²⁶, causing chronic cerebral infection and meningitis.
Laboratory	CSF culture and Serology.
Treatment	<p>Two of the following 3 drugs</p> <ul style="list-style-type: none"> • Tetracycline • Rifampicin • Cotrimoxazole <p>Rifampicin and Cotrimoxazole are preferred as they have good penetration power in the BBB.</p>

²⁰ Polymorphonuclear cells (Neutrophils).

²¹ PMN are significant in Acute Pyogenic Meningitis, however, here we have Lymphocytosis instead.

²² Due to presence of inflammatory substance, dead organism, protein and WBC.

²³ Very similar to TB the main difference is in the history. In brucellosis the history includes exposure to animals.

²⁴ *Brucella Abortus* is also another organism but it is not as common as *Melitensis*.

²⁵ Particularly sheep. Not always the case, sometimes it could be dust particles or aerosol.

²⁶ It will initially cause Bacteremia, then it will go into the brain & cause meningitis.

Tuberculosis²⁷

Etiology	Mycobacterium Species Resist Staining <i>Mycobacterium tuberculosis</i> which infected 1\3 the human race		
Presentation	<ul style="list-style-type: none"> • The patient usually presents with fever of long duration. • Symptoms of cough, and coughing blood (Haemoptysis) when the chest is affected. • It can present as meningitis or cerebral infection with chronic neurological symptoms and signs. • Parenchymal CNS involvement can occur in the form of tuberculoma or, more rarely, abscess. 		
Classification	Intracranial		Spinal
	<ul style="list-style-type: none"> • Tuberculous meningitis (TBM).²⁸ • TBM with Miliary Tuberculosis.²⁹ • Tuberculous Encephalopathy and Vasculopathy. • Single or multiple space-occupying lesions (Tuberculoma). • Tuberculoma with Miliary Tuberculosis. • Tuberculous abscess. 		<ul style="list-style-type: none"> • Pott's spine.³⁰ • Pott's paraplegia.³¹ • Tuberculous Arachnoiditis (myeloradiculopathy).³² • Non-osseous spinal tuberculoma. • Spinal meningitis.
Diagnosis	Clinical ³³	CSF	Imaging ³⁴
	<ul style="list-style-type: none"> • Fever and headache for >14 days. • Vomiting. • Altered sensorium³⁵ or focal neurological deficit. • <u>Mantoux test</u>³⁶ (Tuberculin skin test) 	<ul style="list-style-type: none"> • Microscopy: Z.N. Stain. • Culture: on L.J. or Fluid Medium. • PCR. • Pleocytosis: >20 cells, >60% lymphocytes³⁷. • Increased proteins: >100 mg/dl. • Low sugar: <60%. • Malignant cells: should be -ve. 	<ul style="list-style-type: none"> • Exudates in basal cisterns³⁸ or in sylvian fissure³⁹ hydrocephalus. • Infarcts (basal ganglionic). • Gyral enhancement. • Tuberculoma formation.
Treatment ⁴⁰	<p>For the first 2 months: Rifampicin + Isoniazid (INH) + Ethambutol + Pyrazinamide</p> <p>Then, for 4-6 months: Rifampicin + Isoniazid (INH)</p>		

²⁷ TB can affect anything in your system, including testicals, colon, kidney, eye, vertebrae.

Chronic is usually more than 4 weeks but in TB it's 3 weeks. Communicable disease (can be transmitted). May affect children and be a bit more invasive and reach the brain because his /her immunity is less than the normal adult. The child may present the symptoms of a tumor like palsy, paralysis while the case is TB meningitis. When you start the anti TB treatment they do very well and go back to normal.

²⁸ Located at the base of the skull.

²⁹ Widespread dissemination of Mycobacterium tuberculosis via hematogenous spread.

³⁰ Form of tuberculosis that occurs in the vertebrae.

³¹ Loss of sensory and/or motor function due to the compression.

³² TB causing pain disorder due to the inflammation of the arachnoid.

³³ High white blood cells, usually lymphocytic (same as viral). If someone comes with TB we should also test for HIV.

³⁴ Is very important for diagnosis & follow ups.

³⁵ Sensory function as a whole.

³⁶ The mantoux test is not always correct, sometimes the patient has a disease that suppresses the T cells so the test will come out as negative. That is why we have to check the x-ray and assess the patient clinically.

³⁷ In cases of TB and Brucella.

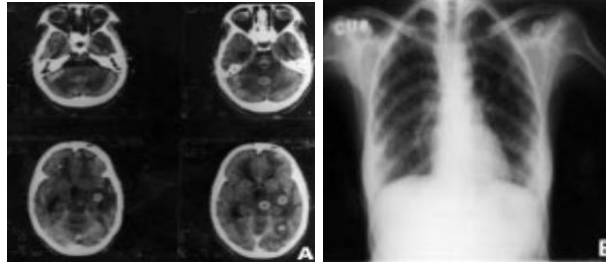
³⁸ MORE.

³⁹ Lateral Sulcus.

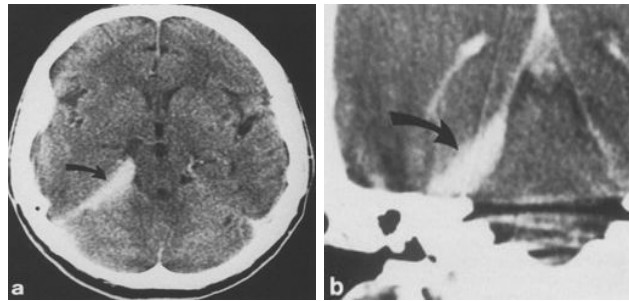
⁴⁰ Like meningitis, sometimes we give them corticosteroids, in chronic infection lots of inflammation is going on so we give it to them to decrease inflammation and to decrease increased intracranial pressure.

Case report⁴¹: disseminated tuberculosis

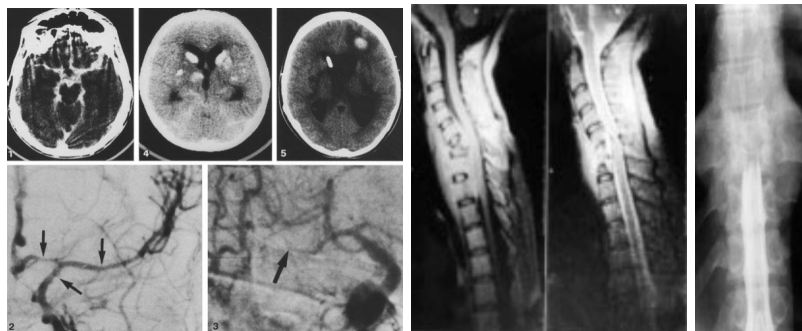
A 30-year-old woman presented with headache, vomiting, fever of 40°C and of being disorientation and inattentive, for 6 days⁴² duration. She was conscious, had lateral rectus palsy along with bilateral papilloedema⁴³. Left plantar was extended. Neck rigidity and Kernig's sign were present. Other systemic and general examinations were normal. All haematological and serum biochemical parameters, including liver function tests, were normal. Chest X-ray showed miliary⁴⁴ shadows in both lungs (figure A) CSF revealed elevated opening pressure, proteins 248 mg/dl, sugar 34 mg/dl (corresponding blood sugar was 98 mg/dl); 204 cells/ml, 15% polymorphs, 85 % lymphocytes⁴⁵. CT head showed multiple small enhancing lesions in brain parenchyma (figure B). The patient was given antituberculous⁴⁶ treatment and corticosteroids⁴⁷. She showed significant improvement in all her symptoms after 15 days.



CT demonstrating Tuberculoma



Spinal block causing compression at the level of T9 vertebra due to a paraspinal abscess (Right)



Intense enhancement of the basal subarachnoid cisterns in acute/subacute TB meningitis (Left)

⁴¹ Typical history of a patient with TB.

⁴² She had acute, severe symptoms during these 6 days but she could of had chronic symptoms in the past few weeks (Neck Rigidity).

⁴³ This means that there is increased intracranial pressure. Possible diagnosis of Acute Pyogenic Meningitis.

⁴⁴ Miliary indicates a hematogenous spread, you will notice small spots in the lungs.

⁴⁵ This means that most likely brain parenchyma.

⁴⁶ Disease in the brain & lungs are 2 types: either malignancy or chronic infection. If its a chronic infection in the brain it's either TB or Nocardia. Since the female is in SA then it's TB.

⁴⁷ When you give steroids to a patient and he/she gets better, this proves the involvement of the immune system as a cause of disease. TB uses the immune system to cause a disease, so to obtain a better result in treatment the anti TB is given with the steroids.

SUMMARY

Chronic cerebral infection

Symptoms	Signs	Causes Of Chronic Cerebral Infection & Meningitis
<ul style="list-style-type: none"> Chronic head ache Neck or back pain Change in personality Facial, arm and leg weakness Double vision, visual loss Clumsiness 	<ul style="list-style-type: none"> +/- Papilloedema → “ICP” Altered mental status, memory loss, etc 3rd, 4th, 6th, 7th Nerve palsy Ataxia Hydrocephalus 	<ul style="list-style-type: none"> <u>Bacterial</u> Tuberculosis / Brucellosis / Nocardiosis / syphilis / Leptospirosis / Lyme disease <u>Parasitic</u> Toxoplasma gondii / T.gambiense / Acanthamoeba spp <u>Fungal & Viral</u>

* Combination of: clinical history + examination finding + Laboratory finding is important to make the right diagnose

Brucellosis “Br.melitensis” → zoonotic “sheep/camels”	Syphilis “Treponema Pallidum” → Sexually-Transmitted
Liptosporosis “ L.Icter haemorrhagia” → contaminated water	Acanthamoeba spp can cause serious eye infections in contact lens wearers because of improper lens handling & poor hygiene
Nocardiosis “N. Asteroids” → Immunosuppressed transplant recipients	
Lyme disease “Borrelia burgdorferi” → hillwalkers / climbers / campers	Toxoplasma gondii → exposure to kittens

The most important causes of chronic bacterial cerebral and meningitic infection in Saudi Arabia are:

1. Tuberculosis “Mycobacterium tuberculosis”	2. Brucellosism “Br.melitensis”
<ul style="list-style-type: none"> Presents with fever of long duration (+/- Haemoptoyis) Parenchymal CNS involvement can occur in the form of tuberculoma It can be intracranial / spinal <u>Imaging</u> <ul style="list-style-type: none"> Exudates in basal cisterns or in sylvian fissure → hydrocephalus Infarcts (basal ganglionic) Gyral enhancement tuberculoma formation <u>Microscopically</u>: Ziehl–Neelsen stain → acid fast bacilli of TB <u>Tests</u>: Mantoux test, Tuberculin skin test (TST) <u>Treatment</u>: <ul style="list-style-type: none"> Start with 4 drugs “for 2 months” Rifampicin + Isonized (INH) + Ethambutol + Pyrazinamide Then: Rifampicin + Isonized (INH) “for 4-6 months” 	<ul style="list-style-type: none"> Affect people who are in contact with domestic animals “Sheep” or those who consume raw milk Can be transmitted sexually & by inhalation Presents with Pyrexia (fever) + night sweating <u>Treatment</u>: Rifampicin + Cotrimoxazole “good penetration power in the blood brain- barrier”

CSF

↑ WBCs “lymphocytosis” - protein is normal or slightly ↑ - glucose is normal or slightly ↓

In chronic meningitis → ↑ CSF pressure → ↑ ICP “due to tuberculoma/brain abscesses”

Multiple Choice and Short Answer Integrated Questions

-To open an answered sheet, please click [here](#)-

CASE - 1

Suleiman, a 53-year-old male was admitted to the ER by his son. The son reports that his father started complaining from a cough that sometimes produces blood two months ago, which did not resolve with coughing syrup. Earlier this week, he started acting clumsy, forgetful, and it was very difficult for him to walk. Vital signs shows a fever of 39°C. On physical examination, Suleiman showed positive Kernig sign and 4th cranial nerve palsy. On MRI, he was negative for cancer, and multiple miliary shadows in the lung were seen.

Which one of the following is your primary diagnosis?

- A. Tuberculosis
- A. Brucellosis
- B. Syphilis
- C. Lyme Disease

Regarding your diagnosis, describe the microorganism's appearance on Gram Stain?

What is the most suitable stain regarding the microorganism of your diagnosis?

Explain the presence of neurological symptoms with Suleiman?

Which of the following is true regarding Suleiman's CBC?

- A. High glucose
- B. Low protein
- C. PMN count is significantly high
- D. Lymphocytosis

Which of the following must be on Suleiman's prescription?

- A. RIF
- B. INH
- C. Cotrimoxazole
- D. A and B

CASE - 2

Sa'ad, a 5-year-old Saudi boy lives in a traditional farm with his parents in Jeizan. Last Monday, he was admitted to the ER by his father. While explaining to the emergency doctor, the father said that Sa'ad had a flu last month, but he was not treated or admitted because the father thought that it would resolve by itself, instead Sa'ad was bed-rested with home remedies. Last night, Sa'ad was not able to sleep due to high temperature, extensive sweating and sharp episodes of headache. The doctor noticed significant mental confusion. Gram Stain of his CSF shows gram negative coccobacilli.

Which one of the following is your primary diagnosis?

- D. Tuberculosis
- B. Brucellosis
- E. Syphilis
- F. Lyme Disease

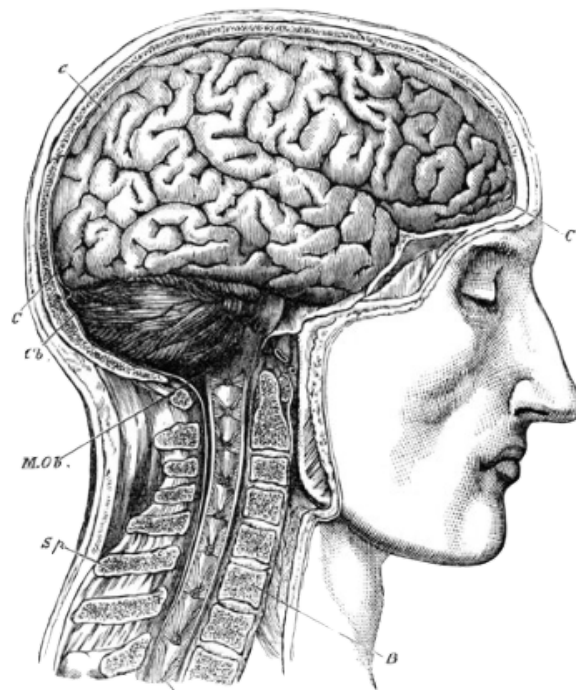
Explain organism of the species causing your diagnosis is the most common in Saudi Arabia?

Explain the route of transmission of the organism associated with your diagnosis:

Which of the following are the most preferable drugs to use in such case?

- A. Cotrimoxazole
- B. INH
- C. Tetracycline
- D. Ethambutol

Explain the reason why did you chose that?



كَذَلِكَ يُبَيِّنُ اللَّهُ لَكُمْ آيَاتِهِ لَعَلَّكُمْ تَعْقِلُونَ ﴿٢٤٢﴾

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Heartful thanks to our phenomenal team members

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