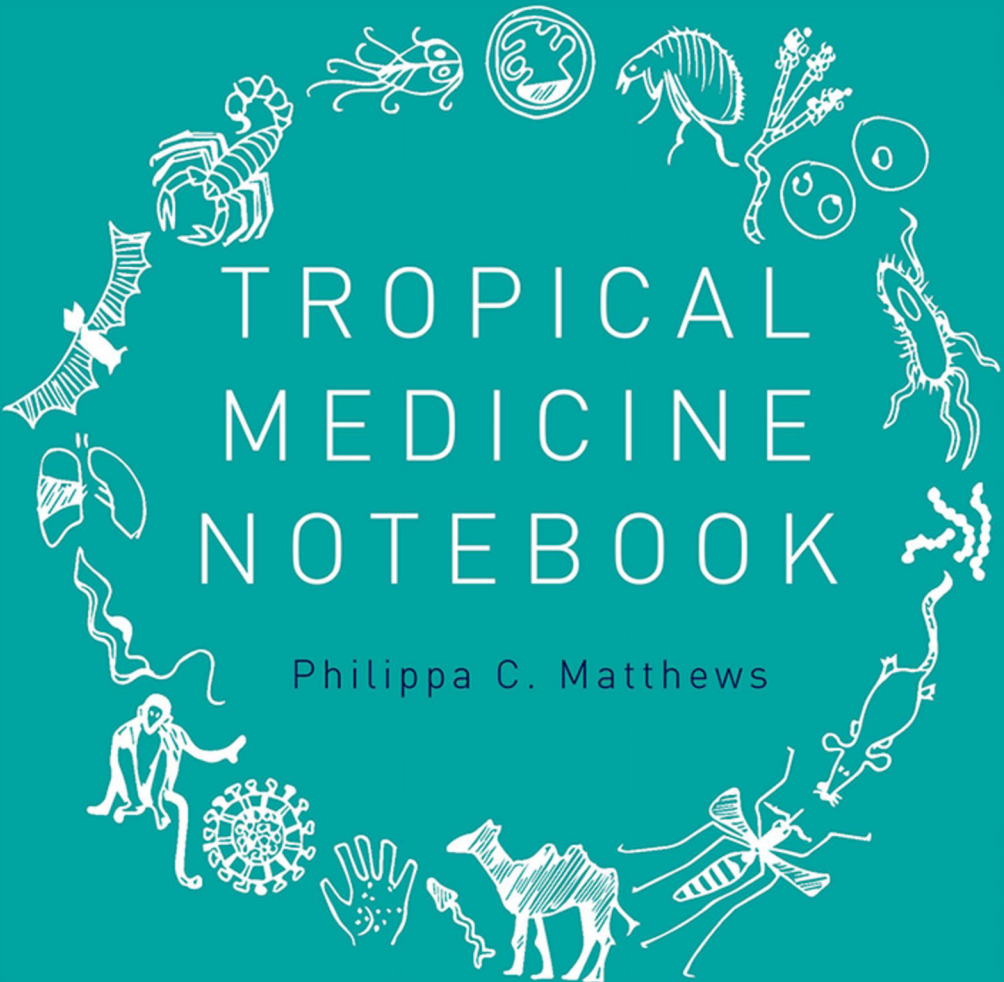


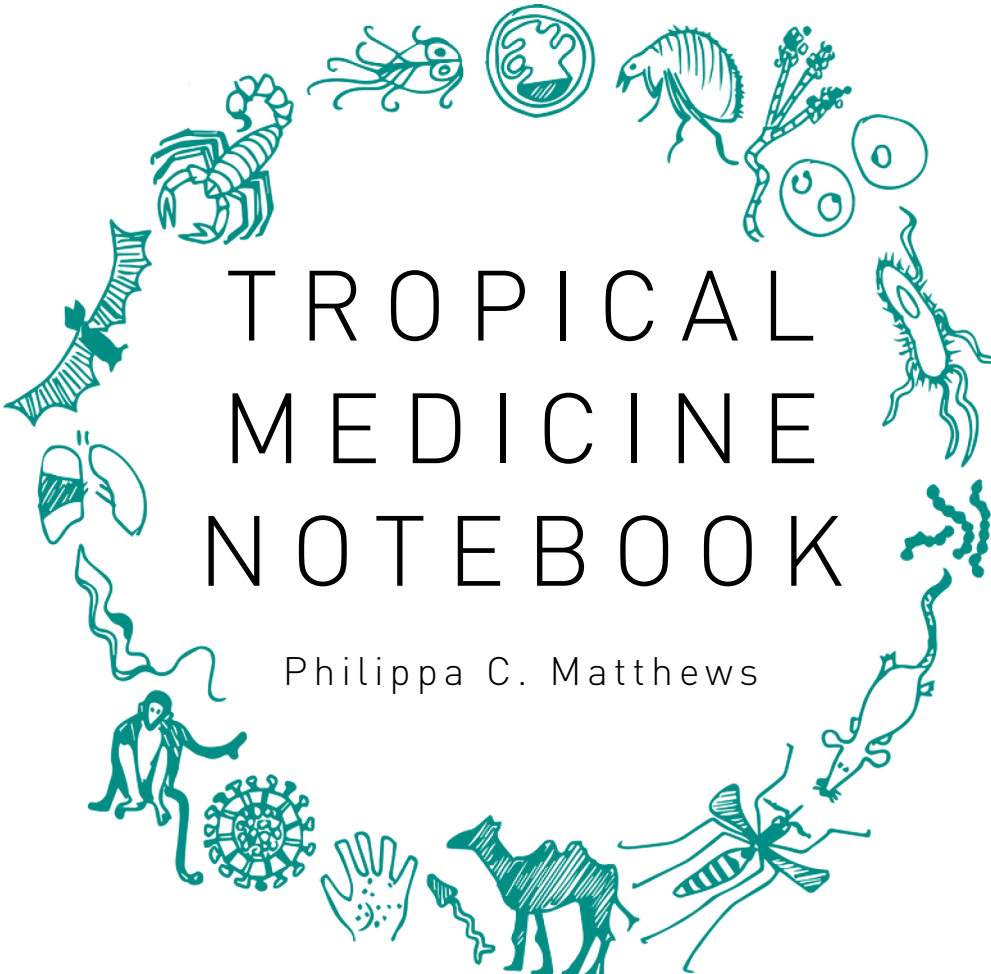
OXFORD



TROPICAL MEDICINE NOTEBOOK

Philippa C. Matthews

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Preface

This book evolved out of a genuine notebook filled with handwritten lists, drawings, and revision jottings assembled while I studied for a Diploma of Tropical Medicine and Hygiene in Liverpool. The notes were expanded during the course of UK-based training in infectious diseases and medical microbiology, and revised through sharing, discussion, and teaching sessions with colleagues. The final volume now bears collective insights from clinical and research practice in tropical and sub-tropical locations, as well as from experiences of travel medicine acquired on home turf in Oxford. My aims have been to make the subject accessible, interesting, and memorable, and to aid learning and understanding by summarizing information in a concise, logical, visual format.

The contents list sets out to reflect the most important topics in infection that may be encountered in the tropics. However, the world is not so simple: 'tropical' infections are exported far afield, ubiquitous pathogens rear their heads irrespective of latitude, and infectious diseases that are endemic in resource-poor settings are relevant concerns for us all. Politics, natural disaster, cultural practice, religion, and economics all feed into the complex dynamics of infection epidemiology. New threats and challenges arise constantly; the contents list was expanded half way through the project to include Zika virus, an organism that has risen from the obscurity of academic virology to being the cause of a major epidemic that has made inter-continental headlines.

The obvious niche for this book is in the teaching, learning, and practice of microbiology and clinical infectious diseases. However, I hope a wider audience will also benefit, as infection is relevant wherever you practise: it presents to diverse care settings with manifestations in any organ system, finds a niche in the setting of chronic disease and malnutrition, leads to sequelae as diverse as blindness, heart failure, and cancer, and produces public health ramifications of major significance for global health.

By its very nature, a 'notebook' approach cannot be exhaustive in its coverage, and the features included vary by section: what may be a crucial feature of one pathogen is not necessarily relevant to another. Of course, clinical care and resources for non-communicable diseases are also hugely important in tropical settings, but this is a subject for another book!

I have aspired to ensure factual content is correct, accurate, and up-to-date throughout. However, please remember that guidelines and recommendations change over time, new diagnostic tests and drug therapies become available, and insights into the complex interplay between host and pathogen are constantly evolving. This book should not be regarded as a comprehensive manual for diagnosis or treatment; for this, you should consult local recommendations, published guidelines, and therapeutic formularies.

It has been a privilege to work on developing this resource, and I hope you enjoy reading, using, and sharing it.

Acknowledgements

I am hugely and particularly grateful to my special friend and colleague, Dr Andy Prendergast, who has championed this project from the outset, was instrumental in the early planning stages, and contributed specifically to the envenomation chapter and the reference list. Without his unique charm, consistent good humour, boundless energy, and engaging optimism, this manuscript would certainly never have seen the light of day.

I would also like to thank Emeritus Professor David Warrell for generously sharing notes and insights on envenomation; I could not have asked for a more esteemed source of wisdom on this topic.

It has been a pleasure to work with Nicola Wilson, Caroline Smith, and Karen Moore at Oxford University Press; I am hugely indebted to them for having the courage to take on this new and unusual challenge, and grateful for everything they have taught me along the way—it has been an amazing journey. Special thanks to Caroline, Karen, and the OUP design team for being so accessible, enthusiastic, and accommodating.

A band of loyal supporters has provided encouragement along the way. Thank you to all those who have participated in review, feedback, and critique of the manuscript, as well as keeping me generally afloat. For their thoughtful and positive suggestions on early manuscript drafts, particular thanks to Howard Moore, Sarah Oakley, and Jo Szram. For moral support, words of wisdom, and sustained optimism throughout this project (and beyond), thank you to Susie Dunachie and Paul Klenerman.

Finally, sincere thanks to three generations of my remarkable family, who constantly delight, inspire, and cheer me on. David, Clare, Andrew, Phoebe, and Rachel, you are my heroes.

Philippa C. Matthews



Mosquito by Phoebe Olubodun

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Abbreviations

>	greater than	GABA	γ -aminobutyric acid
<	less than	GCS	Glasgow coma score
↑	increase	GI	gastrointestinal
↓	decrease	GTT	germ tube test
1°	primary	GU	genitourinary
2°	secondary	HAM	HTLV-associated myelopathy
F	female	HAV	hepatitis A virus
M	male	HBV	hepatitis B virus
20WBCT	20-min whole-blood clotting test	HCV	hepatitis C virus
ALT	alanine aminotransferase	HEV	hepatitis E virus
ARDS	acute respiratory distress syndrome	HLA	human leukocyte antigen
ART	antiretroviral therapy	HPA	Health Protection Agency
ATN	acute tubular necrosis	HSV	herpes simplex virus
BCG	bacillus Calmette–Guérin vaccine	HTLV	human T-cell lymphotropic virus
cAMP	cyclic adenosine monophosphate	IDSA	Infectious Diseases Society of America
CATT	card agglutination test for trypanosomes	INI	integrase inhibitor
CCHF	Crimean–Congo haemorrhagic fever	IV	intravenous
CDC	Centers for Disease Control	JE	Japanese encephalitis
CHIK	Chikungunya	LCMV	lymphocytic choriomeningitis virus
CK	creatinine kinase	LDH	lactate dehydrogenase
CMV	cytomegalovirus	LF	lethal factor
CNS	central nervous system	LFTs	liver function tests
CoV	coronavirus	LPS	lipopolysaccharide
CrAg	cryptococcal antigen	MERS	Middle East respiratory syndrome
CSF	cerebrospinal fluid	MSM	men who have sex with men
CT	computed tomography	NIV	Nipah virus
CVS	cardiovascular system	NNRTI	non-nucleos(t)ide reverse transcriptase inhibitor
CXR	chest X-ray	NRTI	nucleos(t)ide reverse transcriptase inhibitor
DDT	dichlorodiphenyltrichloroethane	NSAIDs	non-steroidal anti-inflammatory drugs
DEC	diethylcarbamazine	PA	protective antigen
DHF	Dengue haemorrhagic fever	PCP	<i>Pneumocystis jirovecii</i> pneumonia
DRC	Democratic Republic of Congo	PCR	polymerase chain reaction
DSS	Dengue shock syndrome	PI/r	protease inhibitor with ritonavir boosting
DVT	deep vein thrombosis	PNS	peripheral nervous system
EEEV	Eastern equine encephalitis virus	RBV	ribavirin
EF	oedema factor	RNA (ss/ds)	ribonucleic acid (single-stranded/double-stranded)
EIA	enzyme immunoassay	RPR	rapid plasma reagin
ELISA	enzyme-linked immunosorbent assay		
ESR	erythrocyte sedimentation rate		
FTA-Abs	fluorescent treponemal antibody absorption test		

RT-PCR	reverse transcriptase PCR	UTI	urinary tract infection
RVF	Rift Valley fever	UV	ultraviolet
SARS	severe acute respiratory syndrome	VDRL	venereal disease research laboratory
SSPE	subacute sclerosing panencephalitis	VEEV	Venezuelan equine encephalitis virus
TB	tuberculosis	VHF	viral haemorrhagic fever
TBE	tick-borne encephalitis	VZV	varicella zoster virus
TNF	tumour necrosis factor	WCC	white cell count
TPHA	<i>Treponema pallidum</i> haemagglutination assay	WEEV	Western equine encephalitis virus
TSP	tropical spastic paraparesis	WHO	World Health Organization
		YF	yellow fever

SECTION 1

Bacterial infections of relevance to the tropics



- 1 Summary of medically important bacteria 3
- 2 Infections caused by Gram-positive bacteria 6
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CHAPTER 1

Summary of medically important bacteria



Classification of bacteria 4

CLASSIFICATION OF BACTERIA



NOTES ON CLASSIFICATION

- Classification is difficult—no single perfect system
- Organisms can be grouped according to:
 - Morphology (shape/staining/structure/motility)
 - Biochemical characteristics (e.g. lactose fermentation)
 - Oxygen requirement (aerobic/anaerobic)
 - Environment or growth requirements (e.g. enteric/fastidious)
 - Antibiotic susceptibility
 - Pathogenicity
 - Genetic sequence (increasingly driving changes to traditional classification)
- The following classification is an amalgamation of commonly recognized approaches to grouping organisms, aimed at devising a system that is logical and easy to remember

GRAM POSITIVE

Gram-positive rods

- *Clostridium* species (see *Clostridia*: Microbiology, p.8)
- *Bacillus* species
- *Corynebacterium* species ('diphtheroids')
- *Actinomyces*
 - *Actinomyces*
 - *Nocardia*
 - *Bifidobacterium*
 - *Propionibacterium*
- Others
 - *Listeria*
 - *Lactobacillus*
 - *Erysipelothrix*
 - *Leuconostoc*

Gram-positive cocci

- Staphylococci
 - Coagulase positive (*Staphylococcus aureus*)
 - Coagulase negative
- Streptococci and enterococci (see *Classification of streptococci* (p.11))
 - Alpha-haemolytic (partial haemolysis of blood agar)
 - Often collectively referred to as '*S. viridans*'; suggests low virulence species such as *S. salivarius*
 - *S. pneumoniae*
 - *S. milleri* group (*S. constellatus*, *S. intermedius*, *S. anginosus*)
 - *S. bovis*
 - Beta-haemolytic (complete haemolysis of blood agar), includes:
 - Lancefield group A (*S. pyogenes*)
 - Lancefield group B (*S. agalactiae*)
 - Lancefield group C (*S. equisimilis*, *S. equi*, *S. zooepidemicus*, *S. dysgalactiae*)
 - Lancefield group D (includes *S. bovis* and *Enterococcus* species)
 - Lancefield groups R and S (includes *S. suis*)
 - Non-haemolytic
- Micrococcus

Mycobacteria

- *Mycobacterium tuberculosis* (see *Tuberculosis*: Microbiology, p.16)
- *Mycobacterium leprae* (see *Leprosy*: Microbiology, p.18)
- Non-tuberculous mycobacteria
 - Fast growing
 - Slow growing

GRAM NEGATIVE

Gram-negative rods

- Enterobacteriaceae (see Chapter 4)
 - Tribe Escherichia (*E. coli*, *Shigella*, *Salmonella*, *Edwardsiella*, *Citrobacter*)
 - Tribe Klebsiellae (*Klebsiella*, *Serratia*, *Enterobacter*, *Hafnia*)
 - Tribe Proteae (*Proteus*, *Morganella*, *Providencia*)
- Pseudomonads
 - *Pseudomonas*
 - *Burkholderia* (including *Burkholderia pseudomallei*; see Melioid: Microbiology, p.27)
 - *Stenotrophomonas*
 - *Comamonas*
 - *Brevundimonas*
- Curved Gram-negative rods
 - *Campylobacter* (see *Campylobacter*: Microbiology, p.34)
 - *Helicobacter*
 - *Vibrio* (see *Vibrio*: Classification, p.32)
 - *Aeromonas*
 - *Plesiomonas*
 - *Spirillum*
- Fastidious
 - 'HACEK group'
 - *Bordetella*
 - *Pasteurella*
 - *Capnocytophaga*
 - *Brucella* (see Brucellosis: Microbiology, p.28)
 - *Francisella*

Coccobacilli

- *Acinetobacter*
- *Yersinia* (see Plague: Microbiology, p.29)
- *Neisseria* (see Meningococcus: Microbiology, p.30)
- *Veillonella*

Spirochaetes (see Chapter 5)

- *Treponema* (see Classification of spirochaetes: Classification, p.36)
- *Borrelia* (see Classification of spirochaetes: Classification, p.36)
- *Leptospira* (see Leptospirosis: Microbiology, p.43)
- *Brachyspira* (see Classification of spirochaetes: Classification, p.36)

Obligate intracellular organisms (see Chapter 6)

- *Rickettsia* (see Rickettsiae: Classification, p.46)
- *Anaplasma/Ehrlichia* (see Classification of intracellular bacteria, p.45)
- *Chlamydia* (see Classification of intracellular bacteria, p.45)
- *Coxiella* (see Q fever: Microbiology, p.49)
- *Bartonella* (see Bartonellosis: Microbiology, p.50)

Anaerobes

- *Fusobacterium*
- *Bacteroides*

NOTES

CHAPTER 2

Infections caused by Gram-positive bacteria



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Tetanus (<i>Clostridium tetani</i>)	9
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Classification of streptococci	11
Pneumococcus (<i>Streptococcus pneumoniae</i>)	12
Group A Streptococcus (<i>Streptococcus pyogenes</i>)	13

ANTHRAX *Bacillus anthracis*

From Greek for 'black'



MICROBIOLOGY

Culture on blood agar:

- White, non-haemolytic, non-motile
- Grows quickly to large 'medusa-head' colonies
- Penicillin sensitive

PATHOPHYSIOLOGY

Pathogenicity is mediated by:

- **Protective antigen (PA)**
 - Binding domain of anthrax toxin
- **Lethal factor (LF)**
 - Combines with PA to cause bleeding, respiratory and cardiac failure
- **Oedema factor (EF)**
 - Adenylate cyclase activity

PREVENTION

- Vaccination (frequent doses required)
- Prophylactic ciprofloxacin (post-exposure)

LIFE CYCLE



Gram $\oplus$
Rod-shaped bacillus
Aerobic



Dormant endospores ('spores')
Resistant to heat/drying/
ultraviolet
Can survive in soil for decades



Ingested by grazing herbivores
(may, in turn, be consumed by
carnivores)



To human by ingestion or
inhalation of endospores (see
Disease syndromes)

DISEASE SYNDROMES

1 Direct inoculation through skin

CUTANEOUS ANTHRAX

Contact with infected animal hide
or meat; also injecting drug users

- Incubation 12 hours–12 days
- > 95% of cases

Papule itching, erythema,
oedema

↓
Vesicle

↓
Eschar black skin lesion

↓
Regional adenopathy

↓
± Chills, headache, sepsis

2 Ingestion of infected meat

OROPHARYNGEAL OR GASTROINTESTINAL ANTHRAX

Severe sore throat
± ulceration, membrane

↓
Neck swelling
massive oedema, dysphagia

↓
Sepsis

(OR)

↓
Nausea and vomiting

↓
**Bloody diarrhoea and bloody
ascites**

↓
Sepsis

3 Inhalation of spores

PULMONARY ANTHRAX +/- MENINGITIS

- N.B. Bioterrorist agent

Fever, myalgia, cough



Severe pneumonia
rapid onset



**Bloody effusions and
haemoptysis**



**+/- Tracheal compression,
mediastinal widening**

(AND/OR)

Haemorrhagic meningitis
~ 100% mortality

TREATMENT

- High dose benzyl-penicillin
and/or ciprofloxacin
- Alternative: doxycycline

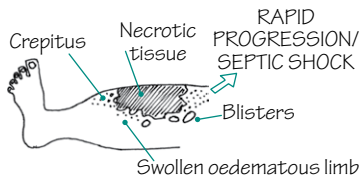
NOTES

CLOSTRIDIA



MICROBIOLOGY

- Gram-positive bacilli (may appear Gram-variable on film)
- Anaerobic, spore-forming
- Produce enzymes (lecithinase, lipase) and toxins
- Can produce hydrogen + nitrogen gas (e.g. 'gas gangrene')



GAS GANGRENE: most often caused by *C. perfringens*

EPIDEMIOLOGY

- Ubiquitous environmental organisms
- > 90 species recognized; < 20 cause human disease (laboratory isolates may be contaminants)
- Spores are highly resistant and persist long term
- Varied clinical syndromes, including:
 - Gastrointestinal infection (food poisoning, diarrhoea, enterocolitis)
 - Skin/soft tissue infection (cellulitis, gas gangrene, myonecrosis)
 - Genital tract infection (post-abortion or post-puerperal sepsis)
 - Pleuropulmonary infection (anaerobic component of mixed infection)
 - CNS infection (anaerobic component of mixed infection)
 - Systemic manifestations of toxin production (e.g. botulism)

BOTULISM *Clostridium botulinum*



PATHOPHYSIOLOGY



Oral subterminal spore highly resistant: can withstand radiation/boiling for several hours

Toxins A-G

- Identical pharmacological effects
- Type-specific antitoxin (or polyvalent antitoxin) required for treatment



Toxin binds irreversibly to block acetylcholine release

Motor blockade

Presenting with:

- Hypotonia
- Ascending flaccid paralysis
- Cranial nerve palsies: ptosis, diplopia
- Impaired speech and swallow
- Cardiac/respiratory failure

5-10% mortality

CLINICAL SYNDROMES

1 Ingestion of preformed toxin

- Typically canned/bottled vegetables; honey

2 Wound contamination

- Organism grows in wound and releases toxin locally
- Episodic outbreaks among injecting drug users

3 Intestinal disease

- Growth of organism in gut with local toxin formation

4 Infant disease

- 'Floppy child' syndrome in infants age < 6 months
- Constipation, listlessness, altered cry, poor feeding, ptosis, ophthalmoplegia

MANAGEMENT

- Urgent airway management: involve intensive care unit early
- Intravenous botulinum antitoxin

NOTES

TETANUS *Clostridium tetani*



MICROBIOLOGY

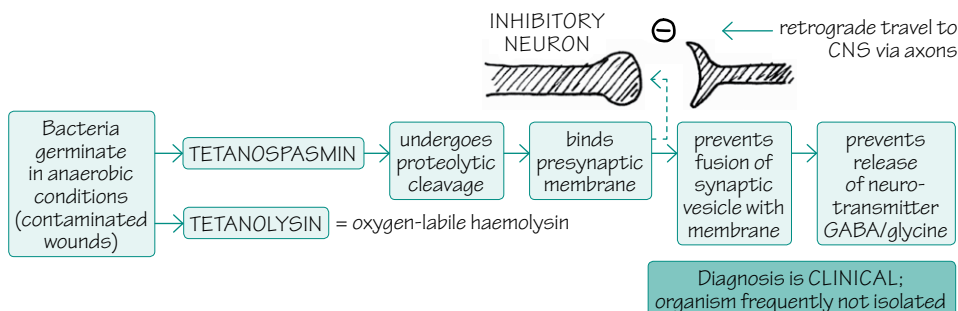
- Gram-positive obligate anaerobe
- Thin film on blood agar due to motility
- Terminal spore: 'tennis racquet' shape
- Highly resistant spores



EPIDEMIOLOGY

- Ubiquitous organism
- Global decline in cases over last 20 years
- Majority of cases: South East Asia and South America
- Commonest in neonates (via umbilicus)

PATHOPHYSIOLOGY



DISEASE SYNDROMES

1 Generalized

- Remember the acronym 'ROAST'
- R** – Rigidity
- O** – Opisthotonus
- A** – Autonomic dysfunction
- S** – Spasms (painful)
- T** – Trismus
- Risk factors
 - Puncture wound
 - Devitalized tissue
 - Delay to debridement
 - Contact with soil or manure
 - Animal bites
 - Clinical evidence of sepsis

2 Neonatal

- Accounts for 50% of cases
- Only in the context of lack of maternal immunity
- 1–10 days postpartum
- Mortality 90%
 - Initially subtle signs: irritability, poor feeding
 - Later spasms, opisthotonus, hypersympathetic state
 - Mental retardation in survivors

3 Localized

- Muscle rigidity near site of injury
- May be mild and persist for months
- Can progress to generalized form: important to recognize and treat

4 Cephalic

- Rare
- Associated with head injury or middle-ear infection
- Incubation 1–2 days
- Presents with cranial nerve palsies

PREVENTION

- ≥ 5 doses of tetanus vaccine (inactivated tetanus toxoid)
- Maternal vaccination protects against neonatal tetanus

MANAGEMENT

- **Debridement:** to clear organism/spores
- **Tetanus immunoglobulin**
- **Antibiotics:** metronidazole/penicillin
- **Benzodiazepines:** to prevent spasms
- **Airway management:** early airway protection ± tracheostomy
- **Manage autonomic instability:** adequate sedation, pacing, atropine
- **Supportive care:** nursing, nutrition, hygiene

DIPHTHERIA *Corynebacterium diphtheriae*



MICROBIOLOGY

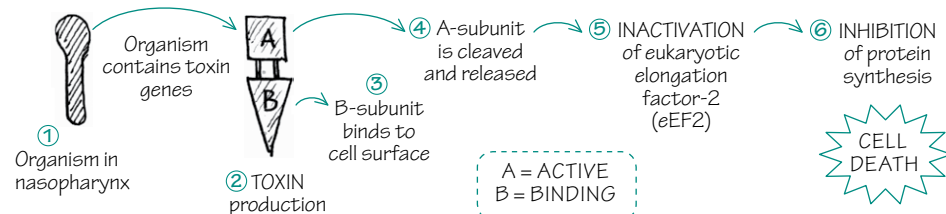
- Gram-positive rods
- Three varieties: var. *gravis*/var. *mitis*/var. *intermedius*
- Family Mycobacteriaceae
- Non-motile, non-sporing, non-branching
- Irregular club-shapes, Y-shapes, 'Chinese letter' arrangements



EPIDEMIOLOGY

- Remains common in developing world
- Can survive for months in the environment
- Spread via naso-pharyngeal secretions
- Incidence highest in young children (3–6 months) after waning of maternal antibody
- Asymptomatic upper respiratory tract colonization is common—reservoir for spread

PATHOPHYSIOLOGY



- Highly potent, heat stable, polypeptide exotoxin; synthesized in high yield in conditions of iron deficiency. Produced locally, then spread via bloodstream to other organs.

DISEASE SYNDROMES

Pharyngeal	CVS	CNS	Skin	Invasive infection
• Nasal discharge • Throat infection with characteristic 'membrane' • Fever, malaise • 'Bull neck' secondary to lymphadenopathy • Stridor	• Myocarditis at 1–2 weeks (as pharyngitis improves) • Electro-cardiogram: ST changes, heart block, dysrhythmias, heart failure, shock	• Local paralysis of pharynx/palate: risk of aspiration • Cranial nerve palsies • Peripheral neuritis (occurs late)	• Chronic non-healing ulcers with grey membranes	(usually non-toxicogenic strains) • Endocarditis • Mycotic aneurysms • Septic arthritis

TREATMENT

- Isolate and barrier nurse
- Penicillin (14 days) or a macrolide
- Antitoxin

PREVENTION

- Purified toxin vaccine, given as part of combined vaccinations, e.g. with tetanus and pertussis (DTP)
- Aim to provide ≥ 5 doses

NOTES