

Inter-Hospital Grand Round

Watch Out!
The Old Foe is Still Around

Background

- ▶ F/75
- ▶ lives alone
- ▶ ADL: independent
- ▶ unremarkable past health
- ▶ NOT on regular follow-up or long-term medication

History of Present Illness

- ▶ repeated fall
- ▶ 1st episode on 19th Dec, 2008
 - slipped & fell while travelled back in Mainland
 - head injury over occipital region
 - no LOC / limb weakness
 - treated with herbs from herbist

Repeated Fall

- ▶ 2nd episode on 29th Dec, 2008
 - tripped over in kitchen at home & fell
 - hit on chin -> bruises
 - no LOC / limb weakness

Attended private hospital on 1st Jan, 2009

▶ Physical Examinations:

- GCS 15/15
- 4–5cm laceration in occipital scalp
 - herbs removed, wound dirty
 - mild surround swelling and redness in surround scalp
- hematoma in right jaw, limited jaw opening
- normal 4 limbs power
 - ROM full

Referral Letter

- ▶ Impression:
 - recurrent fall
 - recent head injury with infected scalp wound
 - chin contusion with hematoma
- ▶ referred to AED

In QEH AED

- ▶ afebrile
- ▶ hemodynamic stable

- ▶ history taking notes ...

“... S/F 2/52 in China with L occipital bleeding, treated by herbist in China

trapped by blanket fell at kitchen, hit on R chin

no LOC, no limb weakness, no sphincter disturbance

neck pain +, L chest wall pain+

no chest pain / palpitation ...”

In QEH AED

- ▶ 3cm laceration over Lt occipital region
- ▶ hematoma over Rt lower mandible
- ▶ tenderness over C-spine +ve

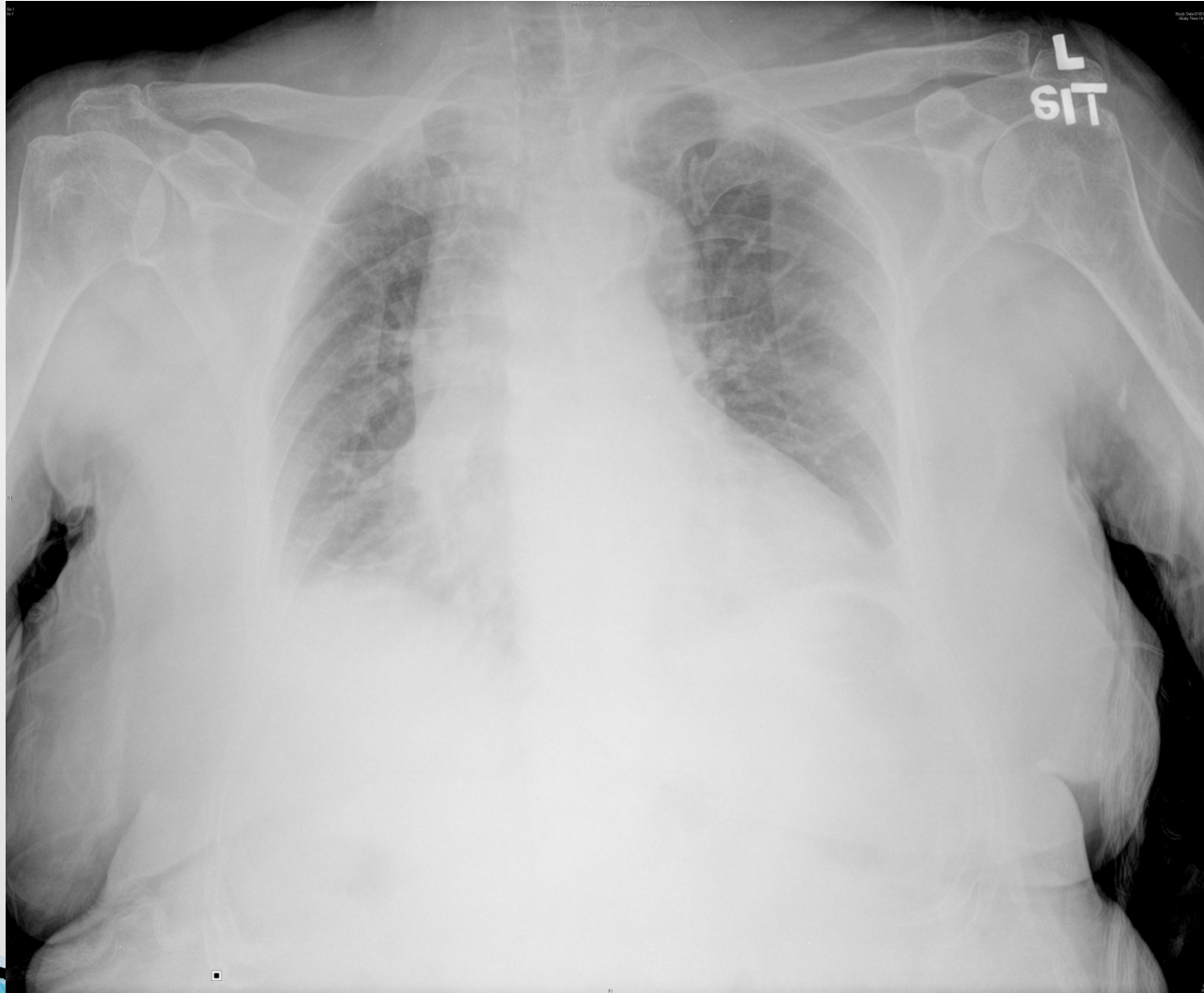
- ▶ GCS 15/15
- ▶ slurring of speech
- ▶ limb power:
 - 5- 5-
 - 5- 5-
- ▶ bilateral planter: down-going

- ▶ no definite sensory deficit
- ▶ no cerebellar sign / wide-base gait

Initial Investigations

- ▶ H'stix: 5.4
- ▶ Hb: 13.7 (11.7 – 14.9 g/dL)
- ▶ wbc: 8.3 (3.7 – 9.2 x 10⁹/L)
- ▶ plt: 241 (145 – 370 x 10⁹/L)
- ▶ Na: 142 (136 – 145 mmol/L)
- ▶ K: 3.7 (3.5 – 5.1 mmol/L)
- ▶ urea: 11.4 (3.0 – 7.4 mmol/L)
- ▶ Cr: 93 (47 – 82 μ mol/L)
- ▶ Ca: 2.16 (2.10 – 2.62mmol/L)
- ▶ bil, total: 22 (5 – 27 μ mol/L)
- ▶ ALP: 88 (53 – 141 IU/L)
- ▶ ALT: 29 (8 – 36 IU/L)
- ▶ CXR, X-ray C-spine & Rt mandible ordered

Chest X-ray



X-ray Rt mandible



X-ray Cervical Spine



In QEH AED

- ▶ provisional dx:
 - recurrent fall
- ▶ management:
 - put on safety vest & transferred to observation ward

In Observation Ward

- ▶ CT Brain:
 - no abnormality detected
- ▶ referred physiotherapist for walking exercise
- ▶ *“... noticed decreased oral feeding with fair jaw movement ...”*
 - intravenous fluid given
 - dental team consulted for
 - ? dislocation of TM joint

In Observation Ward on 2nd Jan

- ▶ Dental Team notes –
 - ecchymosis over chin
 - no hematoma over floor of mouth
 - no dislocation of TM joints
 - no maxillo-mandibular bony fracture
- ▶ admitted to medical ward
 - frequent fall
 - functional decline – oral feeding not tolerated

In Medical Ward on 2nd Jan

- ▶ afebrile
- ▶ BP: 148/87mmHg
- ▶ pulse: 101bpm
- ▶ SpO2 (RA): 92% → SpO2 (2L): 96%

- ▶ GCS: 15/15
 - ? slurring of speech

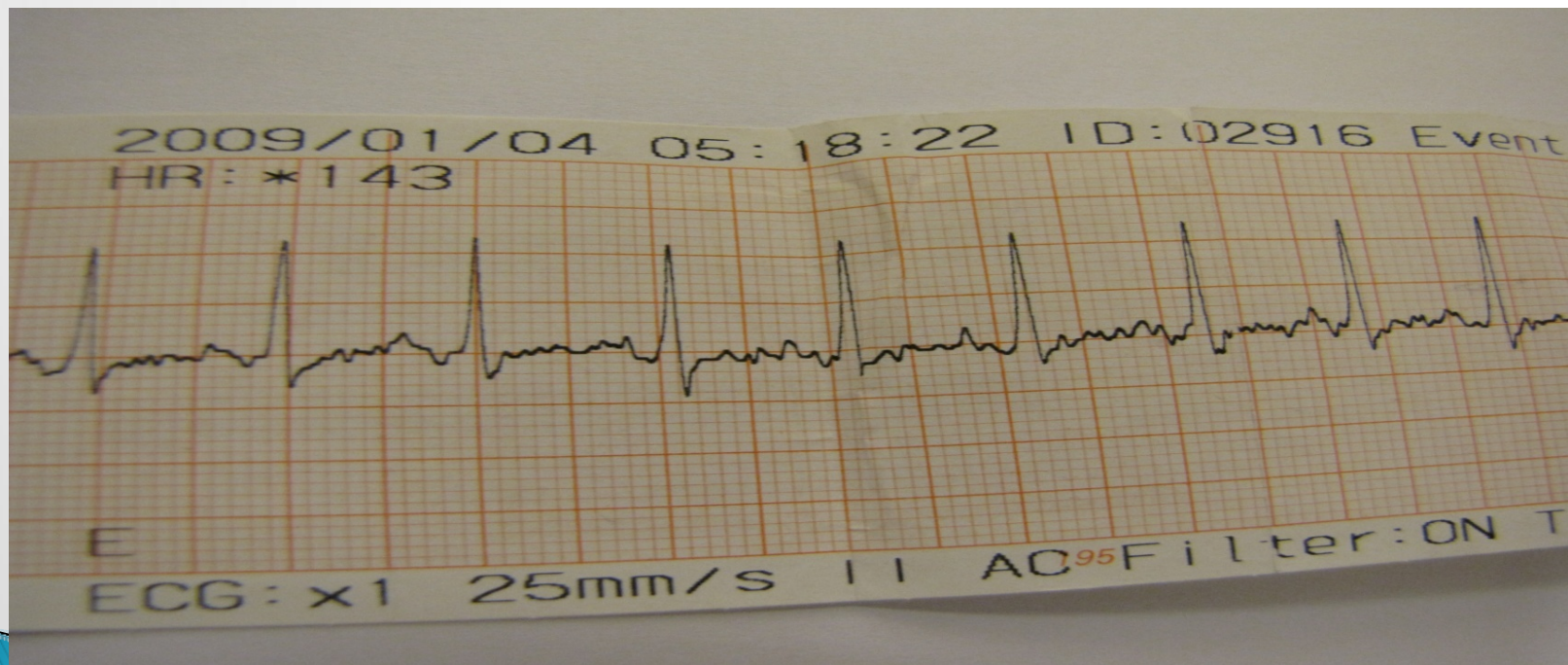
 - increased bilateral upper limb tone
 - decreased Lt upper limb & Rt lower limb power due to ? pain
 - bilateral planter: down-going

In Medical Ward on 2nd Jan

- ▶ suspected CVA
 - Aspirin added
- ▶ NPO except medication – only mild jaw movement
 - referred speech therapist
- ▶ Holter study arranged
 - repeated fall
- ▶ Augmentin empirically started
 - ? infected jaw hematoma & occipital wound

In Medical Ward on 4th Jan

- ▶ patient complained of
 - generalize muscle cramping
 - shortness of breath
 - sweating



In Medical Ward on 4th Jan

- ▶ neck rigidity
- ▶ decrease limb power over 4 limbs
- ▶ suspected dystonia
 - urine toxicology saved
 - lumbar puncture
 - opening pressure: 12cm H₂O
 - clear CSF
 - CSF protein: 0.53 (0.15 – 0.45 g/L)
 - CSF glucose: 6.1 (2.3 – 4.7 mmol/L)
 - wbc: 6/cmm
 - gram stain: no organism seen
- ▶ respiratory distress with increasing oxygen requirement
 - SpO₂ (6L mask): 95%

Differential Diagnosis?

- ▶ acute cerebrovascular accident?
- ▶ CNS infection?
- ▶ acute dystonia?
 - related to drugs / herbs

ICU Consultation on 4th Jan

▶ GCS: E4V1–2M6

- obey commands with eye blinking & closing
- incomprehensible sounds due to locked jaw
- trismus +++
- spasm of neck muscle
- hyper-extended neck
- increase limb tone (upper limb > lower limb)

Clinical Diagnosis

Tetanus

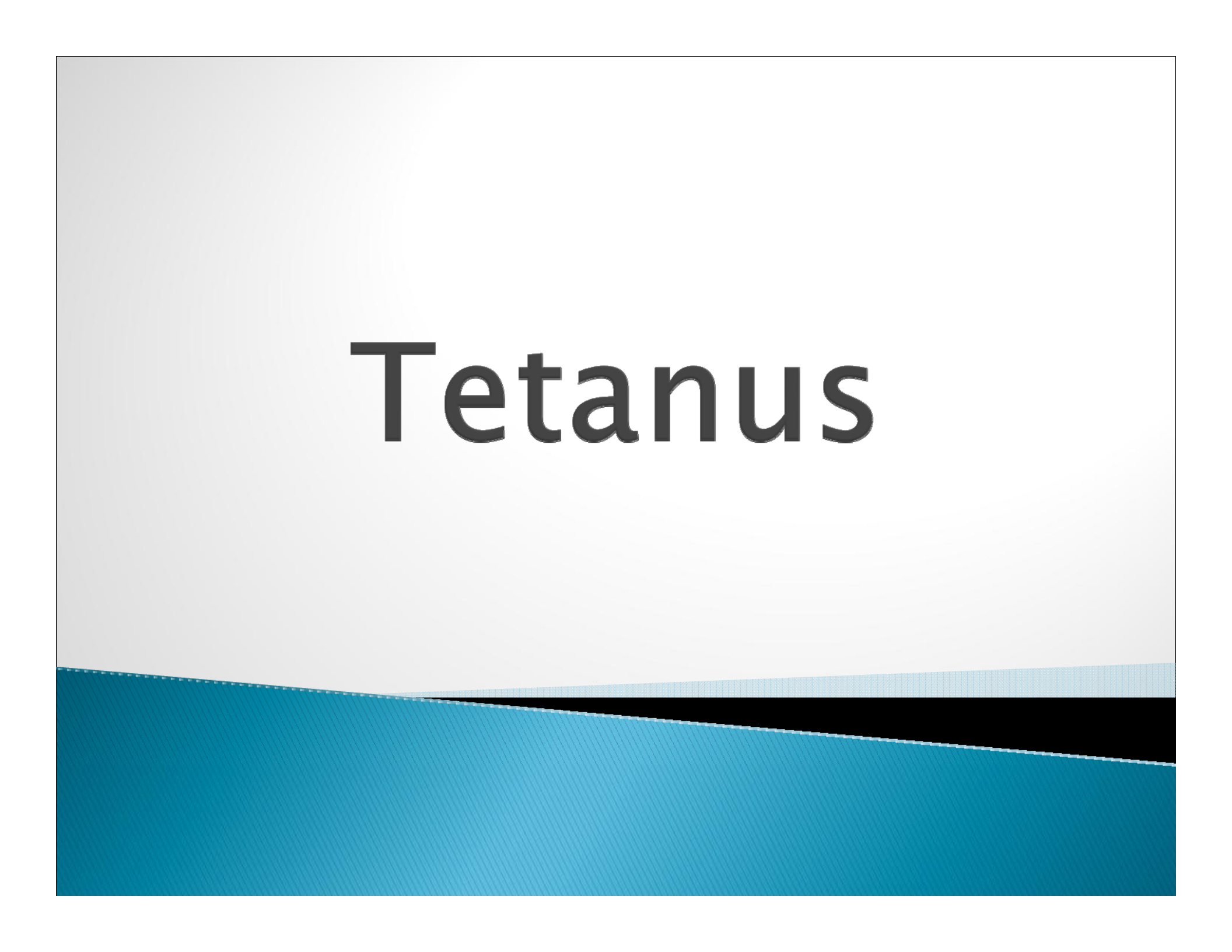
ICU Consultation

- ▶ diaphoresis & distress
 - BP: 200/110mmHg
 - pulse: 140bpm
 - SpO2 (100% mask): 94–96%
 - RR ~ 30–40/min
- ▶ sputum sound with poor coughing effort

Airway Management ...

- ▶ excepted difficult airway
- ▶ anesthetist consulted
 - awake fibre-optic bronchoscopy
 - intra-operative findings:
 - difficult to get clear FOB view due to vigorous respiration
 - vocal cords seen with no significant swelling
 - size 6.0 endotracheal tube inserted via Rt nostril
 - direct laryngoscope with McCoy Blade – grade 3 larynx
- ▶ Transferred to ICU for ventilatory support

Tetanus

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Tetanus

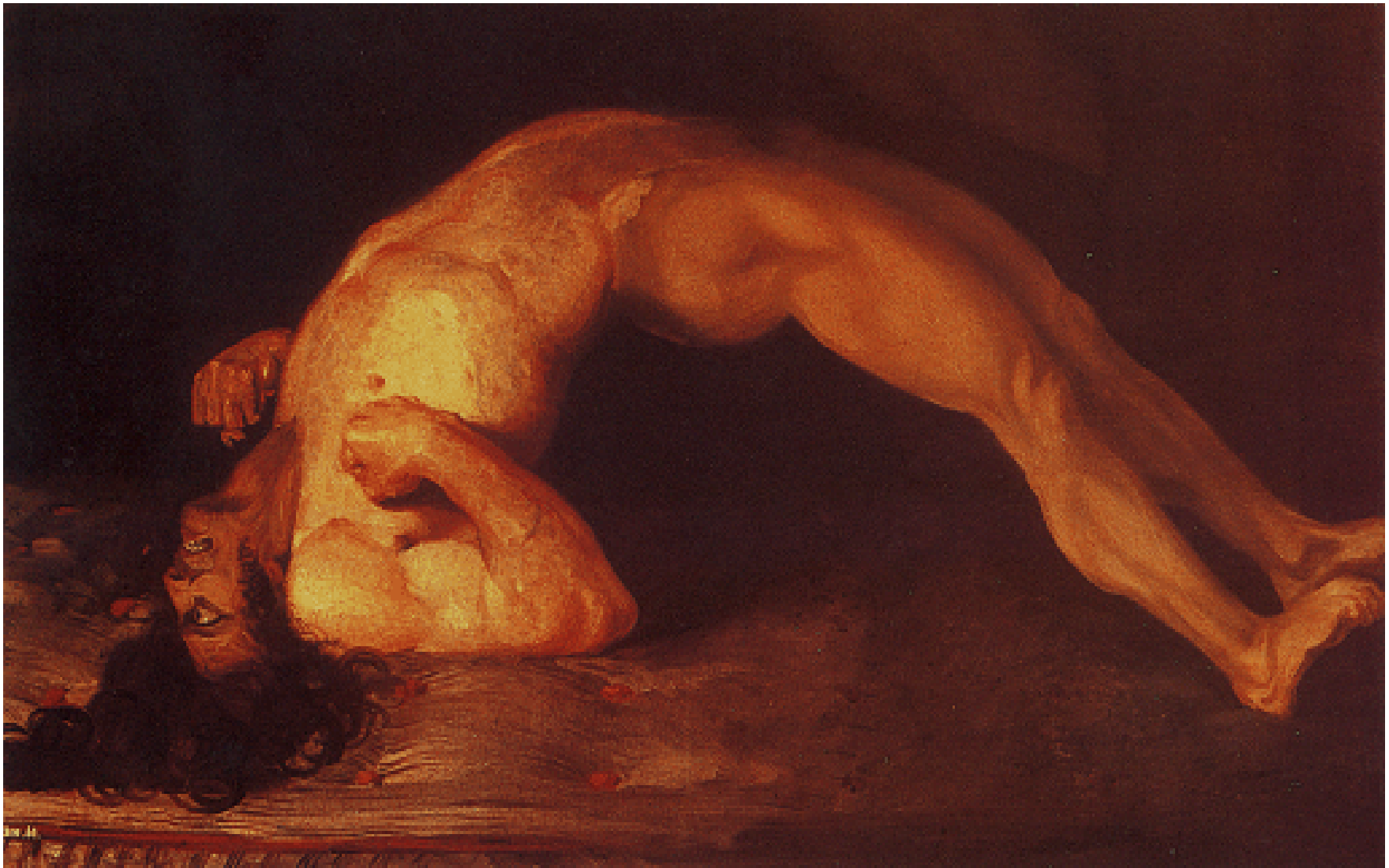
- ▶ derives its name from the Greek word “tetanos”
 - meaning to contract
- ▶ preventable, 3rd – World disease
- ▶ acute, often fatal disease
- ▶ caused by an exotoxin produced by *Clostridium tetani*
- ▶ characterized by
 - generalized muscle rigidity
 - autonomic instability
 - convulsions
- ▶ NOT contagious

Tetanus – Background

- ▶ records containing clinical descriptions of tetanus (5th century BC)
- ▶ first described by Hippocrates
- ▶ Carle & Rattone first produced tetanus in animals in 1884
 - injection with pus from a fatal human tetanus case
- ▶ Nicolaier produced tetanus in animals
 - injecting them with soil
- ▶ Kitasato isolated the organism in 1889
 - toxin could be neutralized by specific antibodies

Tetanus – Background

- ▶ Nocard demonstrated the protective effect of passively transferred anti-toxin in 1897
- ▶ passive immunization
 - treatment & prophylaxis during World War I
- ▶ Descombey developed tetanus toxoid in 1924
 - first widely used during World War II
- ▶ despite widespread immunization, tetanus remains a major public health problem in the developing world
 - reported cases in the developed world



Sir Charles Bell's portrait of a man with generalized tetanus and evident opisthotonos and risus sardonicus
(Original in the Royal College of Surgeons of Edinburgh, Scotland)

Pathogenesis

The background of the slide is an abstract composition. The top half is a light gray gradient. The bottom half is divided into two sections: a dark blue textured area on the left and a black horizontal band on the right. The word "Pathogenesis" is centered in the gray area.

Tetanus – Pathogenesis

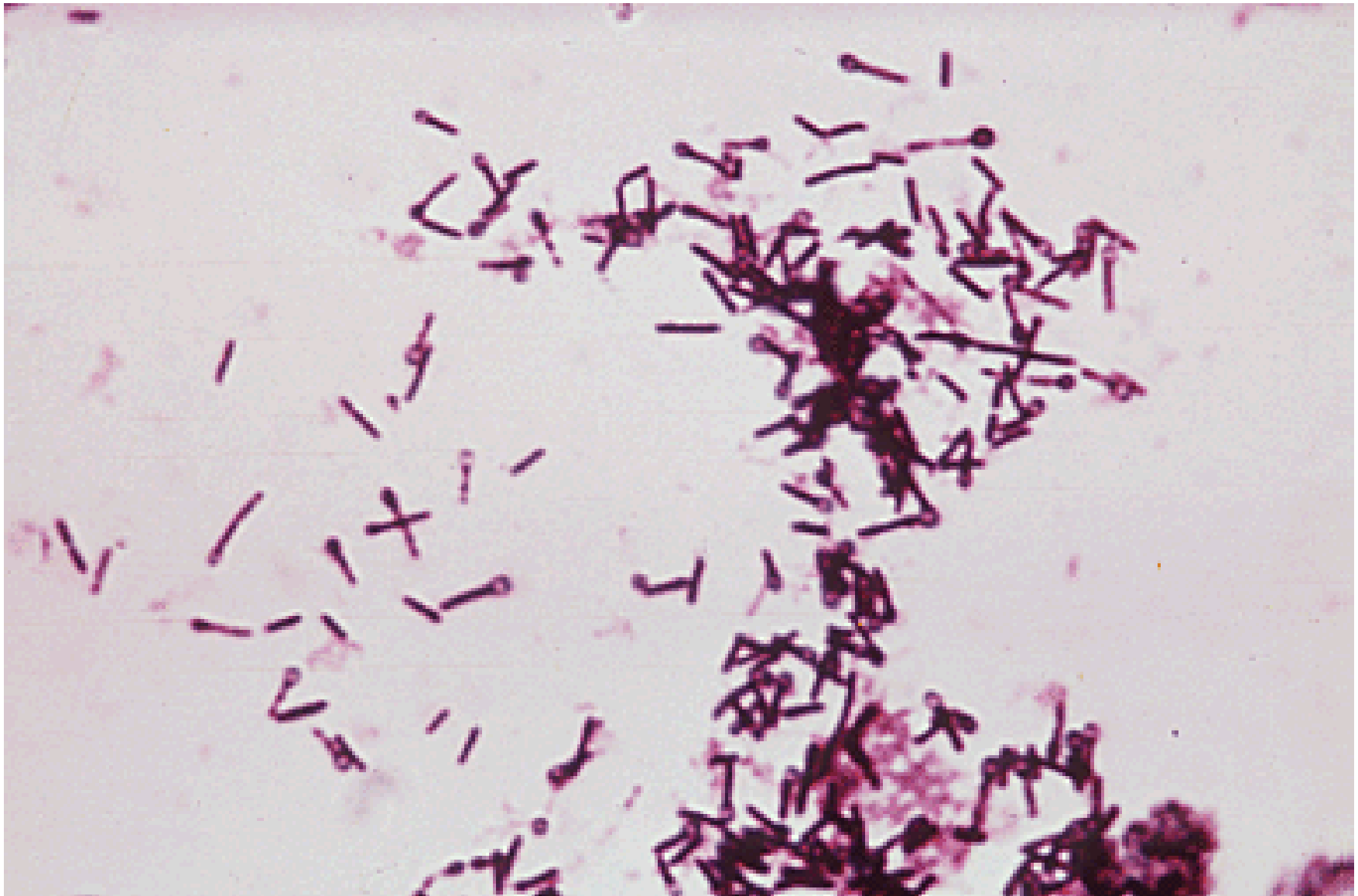
▶ *Clostridium tetani*

- obligate anaerobic gram-positive bacillus
- non-invasive
- forms spores
 - resistant to heat (can survive autoclaving (121°C) for 10–15 minutes) & the usual antiseptics
 - exist ubiquitously in soil, house dust, animal intestines & human feces

▶ usual mode of entry is through puncture wound or laceration

- injury is often trivial
- no evidence of wound – 20%





Clostridium tetani

Tetanus – Pathogenesis

- ▶ spores proliferate after gaining access to devitalized tissue
- ▶ 2 exotoxins

1) Tetanospasmin

- acts at several sites
- accounts for clinical manifestation

2) Tetanolysin

- little clinical importance

Tetanus – Pathogenesis

▶ Tetenospasmin

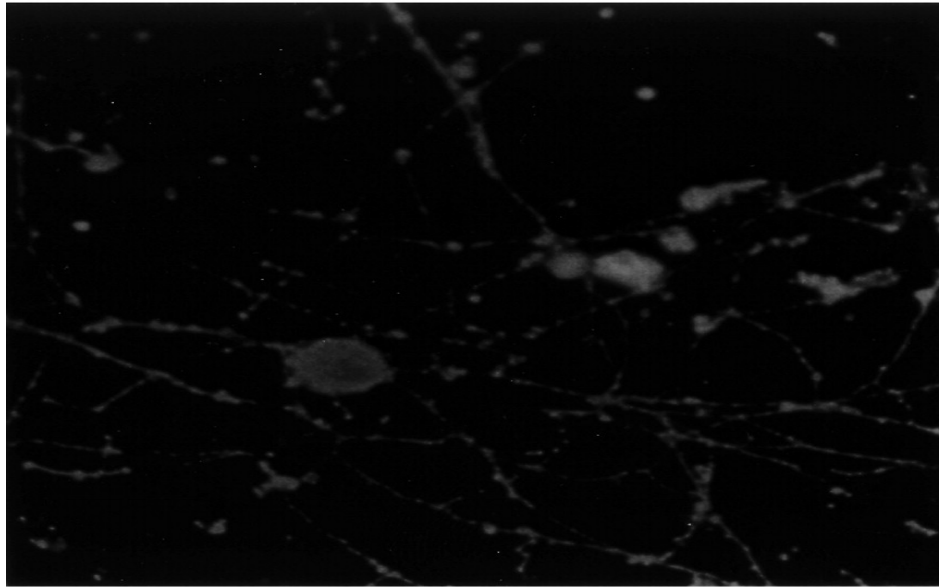
- one of the most potent toxins known
 - minimum lethal dose – 2.5 nanograms/kg
 - estimated 240 grams could kill the entire world population

▶ neurotoxin

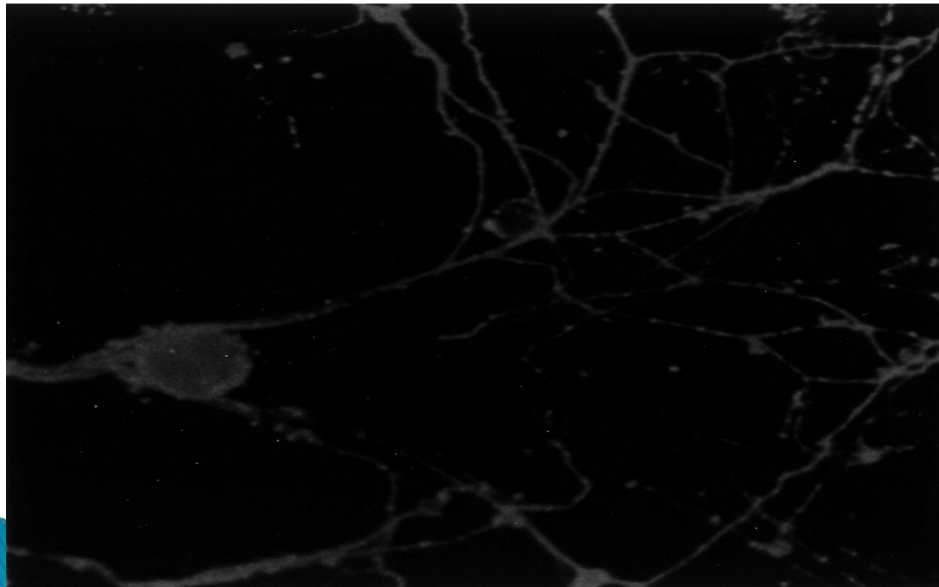
- distributed via lymphatic & vascular circulations to the end-plates of all nerves
- enters the peripheral nervous system (PNS) at the myoneural junction
- transported centripetally into neurons of the central nervous system (CNS)
- affected neurons – incapable of neurotransmitter release

Tetanus – Pathogenesis

- ▶ spreads to all neurons
- ▶ neurons – **gamma-aminobutyric acid (GABA) & glycine** (major inhibitory neurotransmitters)
 - particularly sensitive to tetanospasmin
 - failure of inhibition of motor reflex responses to sensory stimulation
- ▶ generalized / unopposed contractions of both agonist & antagonist musculature
 - tetanic spasm
- ▶ shortest peripheral nerves – first to deliver the toxin to the CNS
 - facial distortion
 - back & neck stiffness



MBP-TC₂₇₁₋₄₅₁



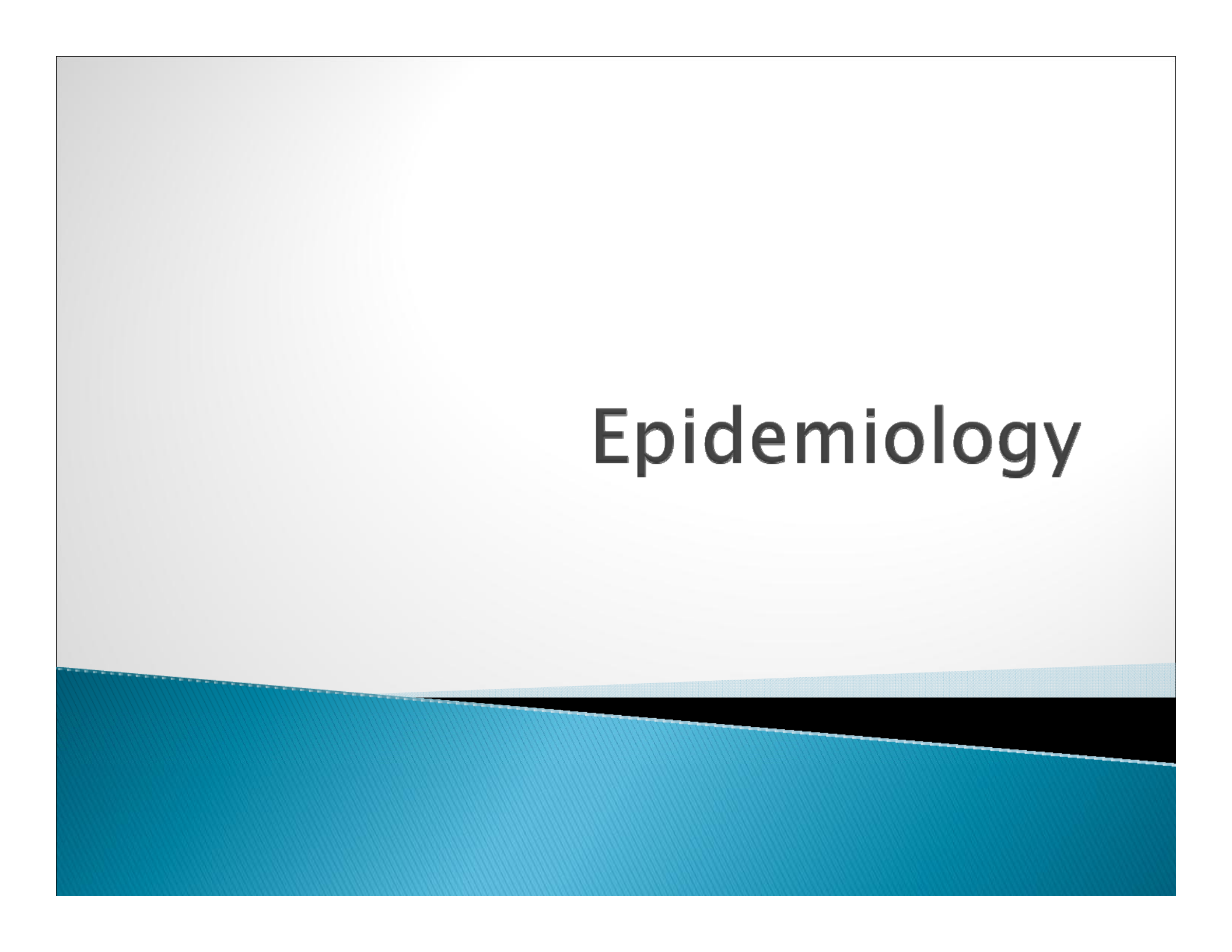
FRAGMENT C

Radio-labelled fragment C of tetanus toxin in the dorsal root ganglion showing tetanus toxin within axons and nerve cell bodies
(Dr N. Fairweather –
Department of Biochemistry,
Imperial College, London)

Tetanus – Pathogenesis

- ▶ **spinal cord**
 - dysfunction of polysynaptic reflexes
- ▶ **brain**
 - seizure
 - inhibition of cortical activity
 - autonomic dysfunction
- ▶ **once toxin fixed to neurons**
 - cannot be neutralized with anti-toxin
- ▶ **recovery of nerve function**
 - ▶ sprouting of new nerve terminals
 - ▶ formation of new synapses

Epidemiology

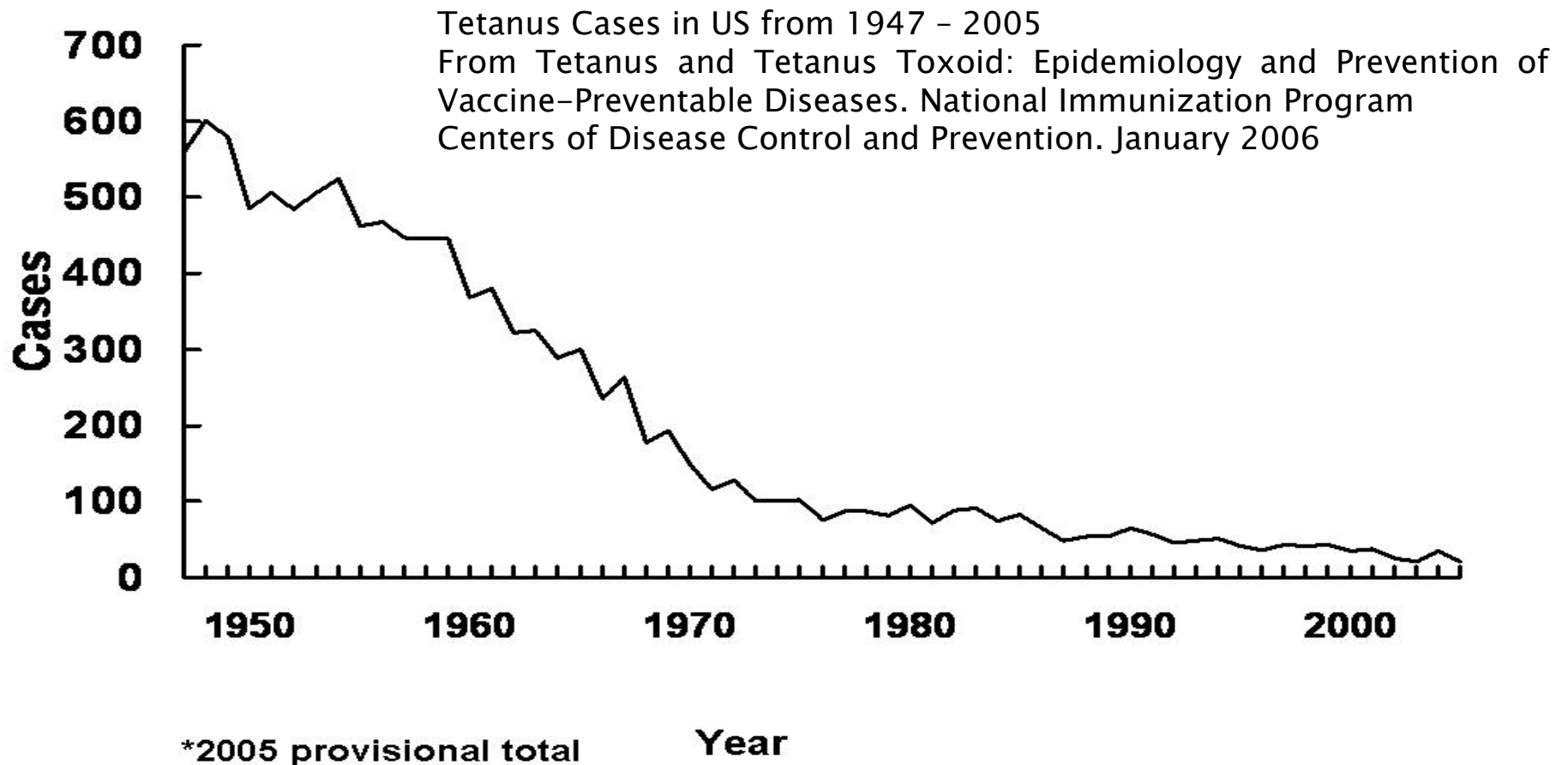
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Tetanus – Epidemiology

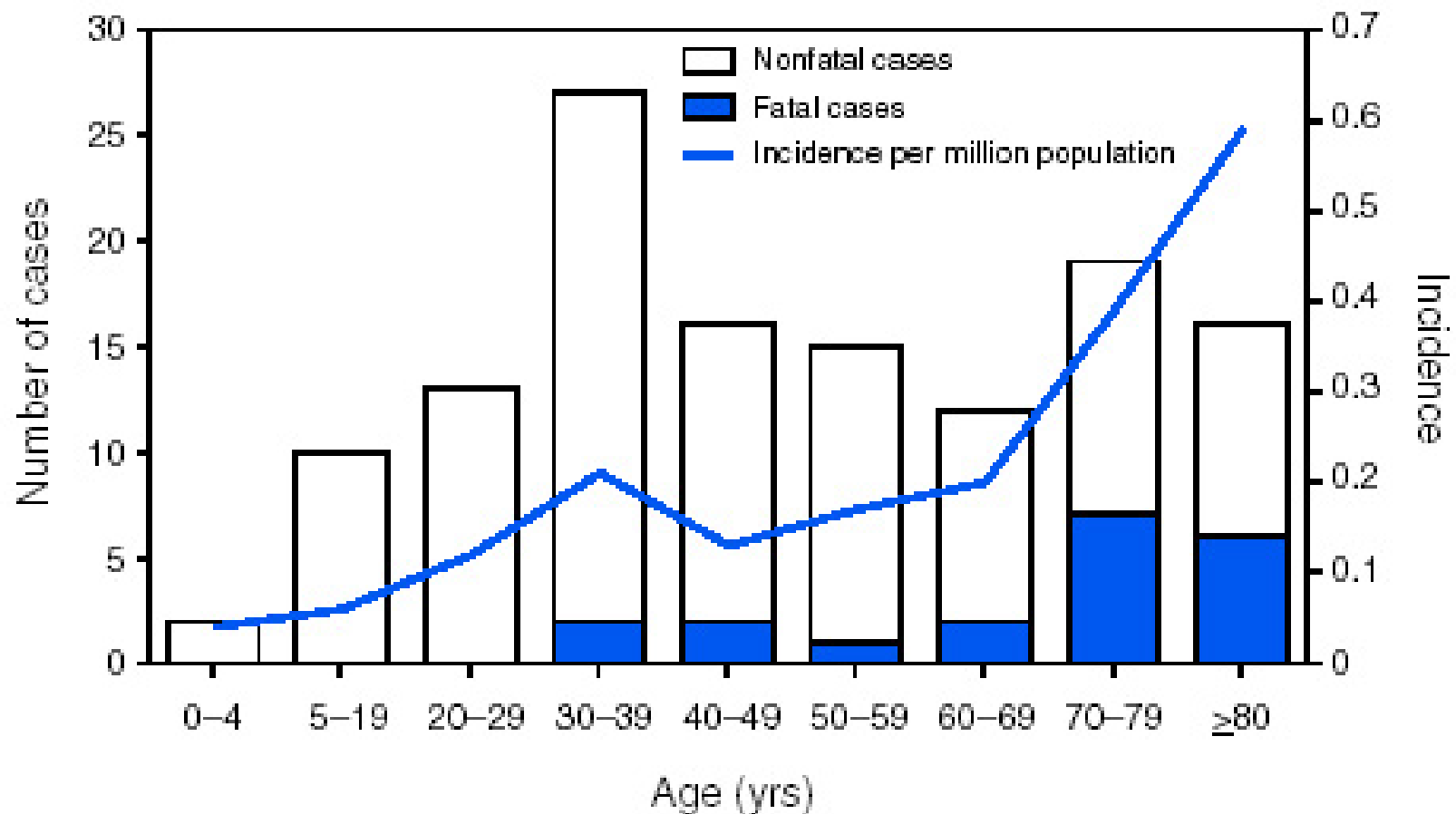
- ▶ tetanus – disease of the elderly & debilitated in developed countries
 - as younger people likely to have been immunized
- ▶ United States – incidence of tetanus declined substantially since the mid 1940s
 - 0.23 per 100,000 in 1955
 - 0.04 per 100,000 in 1975

Tetanus – Epidemiology

Tetanus—United States, 1947-2005*



Tetanus – Epidemiology



“Number of Tetanus Cases Reported, Average Annual Incidence Rates, and Survival Status of Patients, by Age Group.” Pascual FB, McGinley EL, Zanardi LR, et al: Tetanus Surveillance – United States, 1998–2000. *MMWR Surveill Summ.* 2003 Jun 20; 52(3): 1–8

Tetanus – Epidemiology

- ▶ worldwide, tetanus is predominantly a disease of underdeveloped countries
 - poor hygiene & medical services
- ▶ affects all age groups
 - in 1992, an estimated 578,000 infant deaths occurred due to neonatal tetanus
 - in 1998, 215,000 deaths occurred with more than 50% of these on the Africa continent
- ▶ the annual incidence of tetanus – 0.5 – 1 million cases
- ▶ World Health Organization (WHO) Expanded Program on Immunization

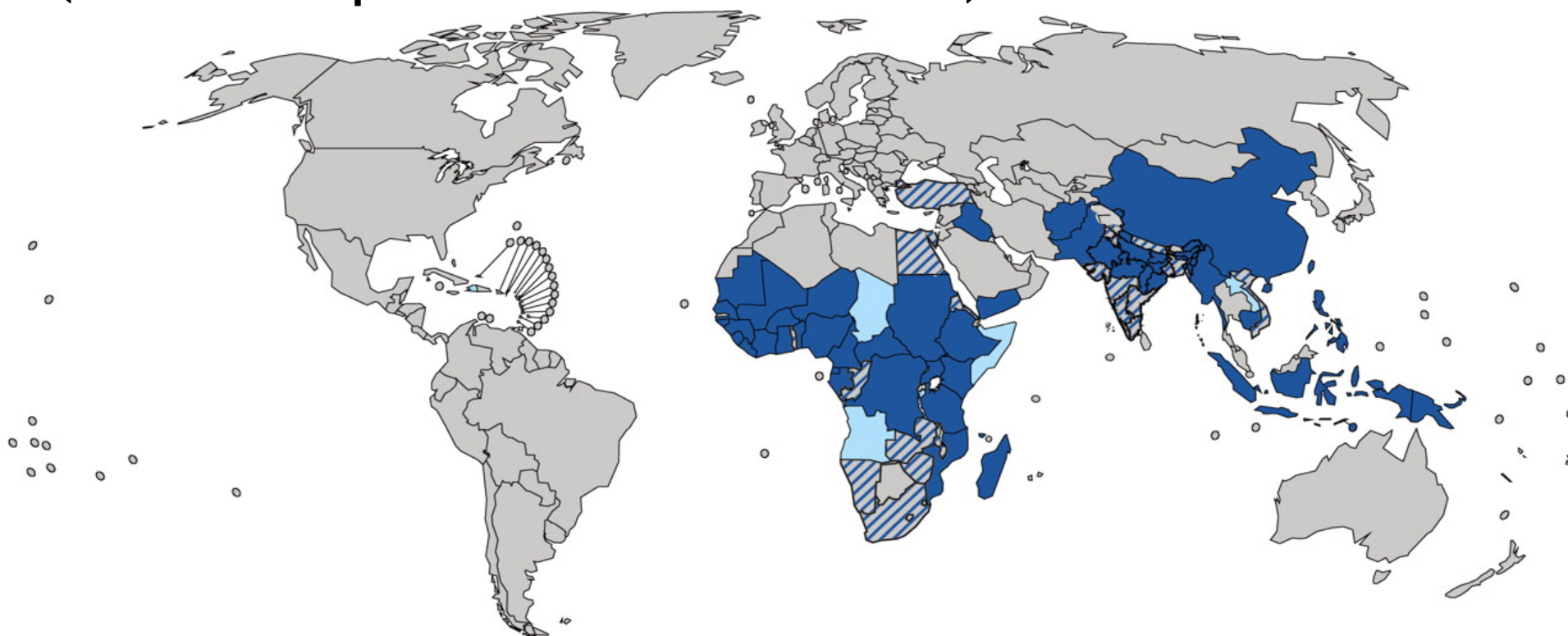
2008 global figures

16,628 reported cases

163,000 estimated deaths (in 2004)

82% estimated DTP3 coverage

Situation of Maternal and Neonatal Tetanus (Remains a problem in 51 countries)



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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	MNT eliminated prior to 2000 (<i>135 countries</i>)
	MNT eliminated since 2000 (<i>14 countries & 15 States in India</i>)
	MNT eliminated in 50% - 99% of districts (<i>38 countries</i>)
	MNT eliminated in < 50% of districts (<i>6 countries</i>)

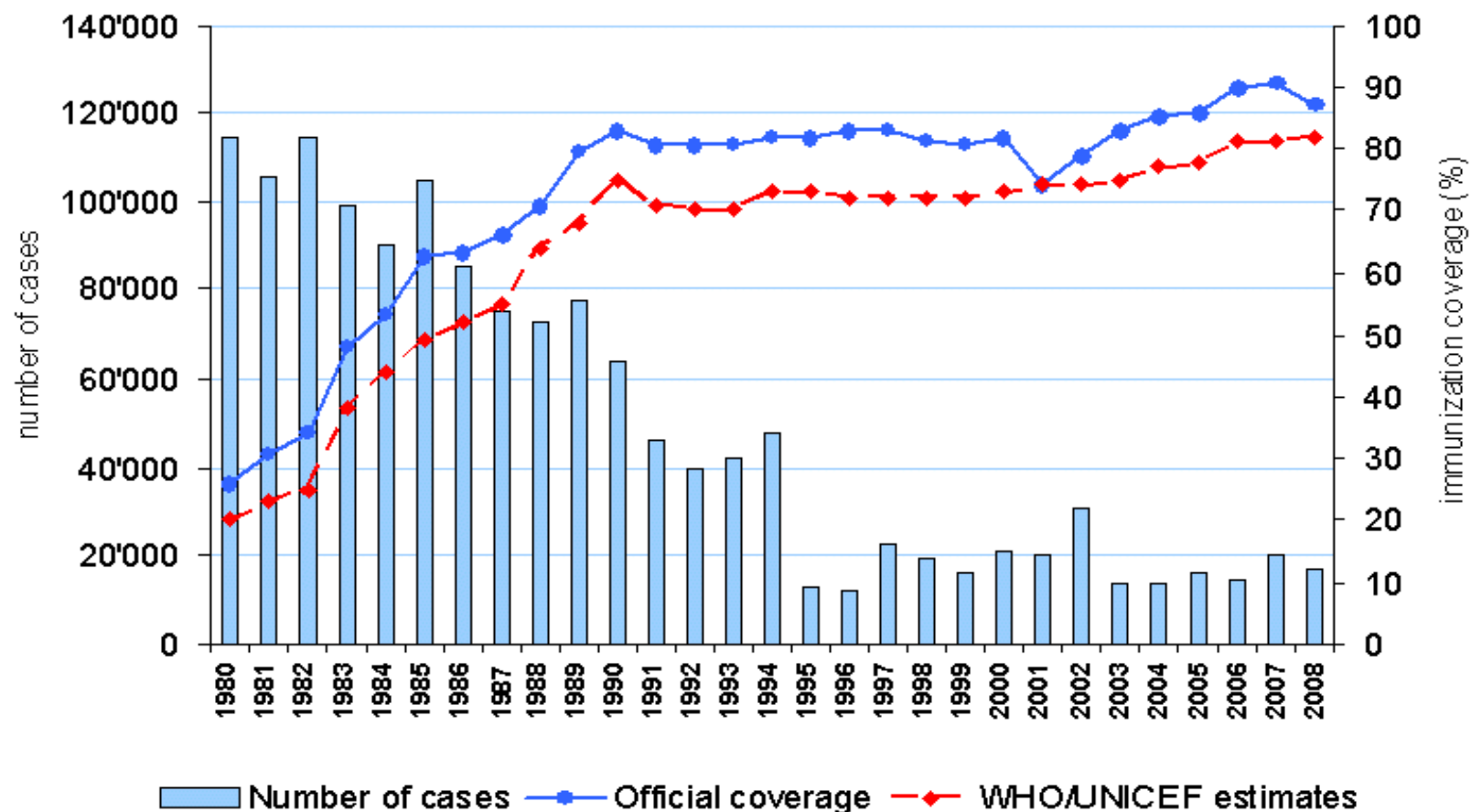
Source: WHO/UNICEF estimates and WHO/IVB database, April 2009

193 WHO Member States. Data as of April 2009



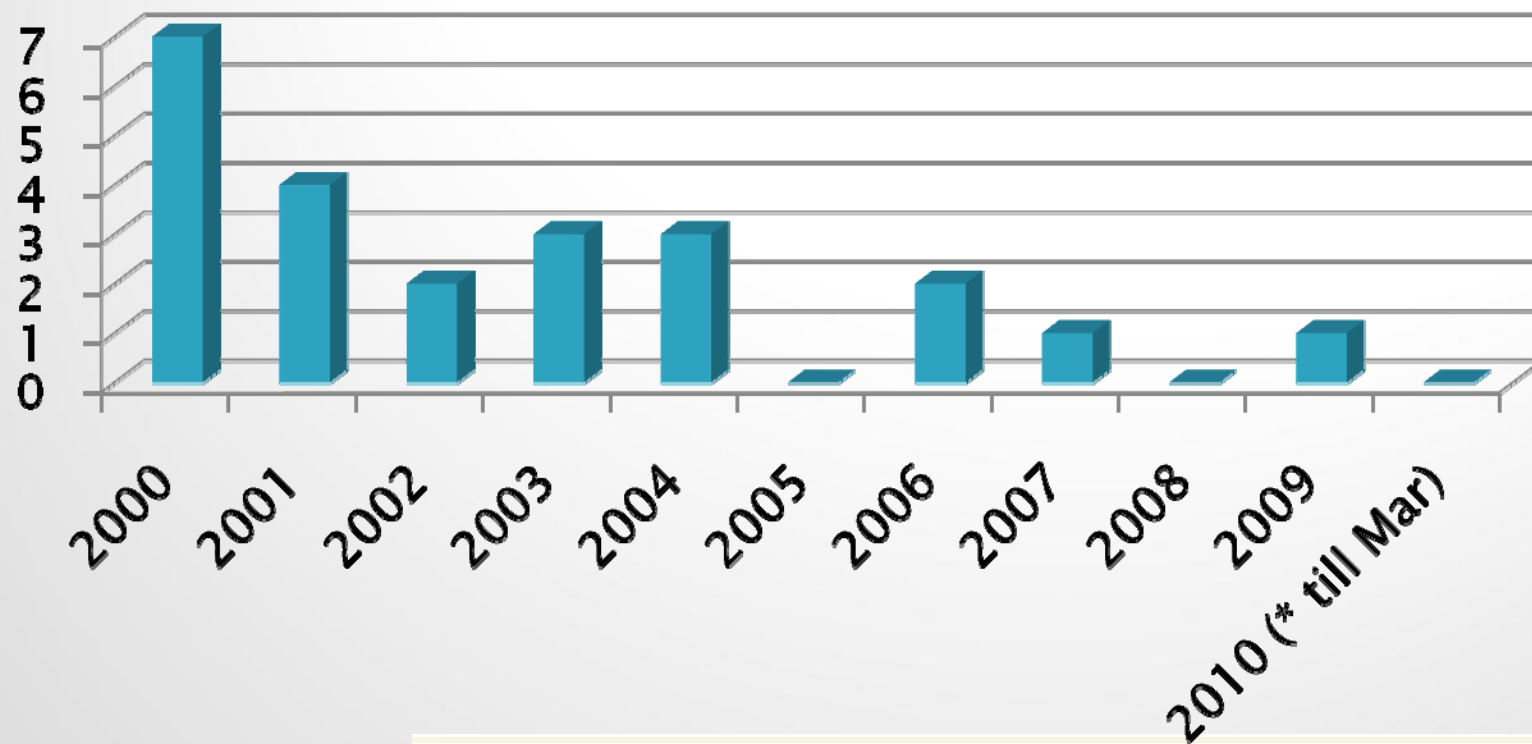
Tetanus – Epidemiology

Total tetanus global annual reported cases and
DTP3 coverage, 1980-2008



Epidemiology – Local Data

Number of Cases – Tetanus

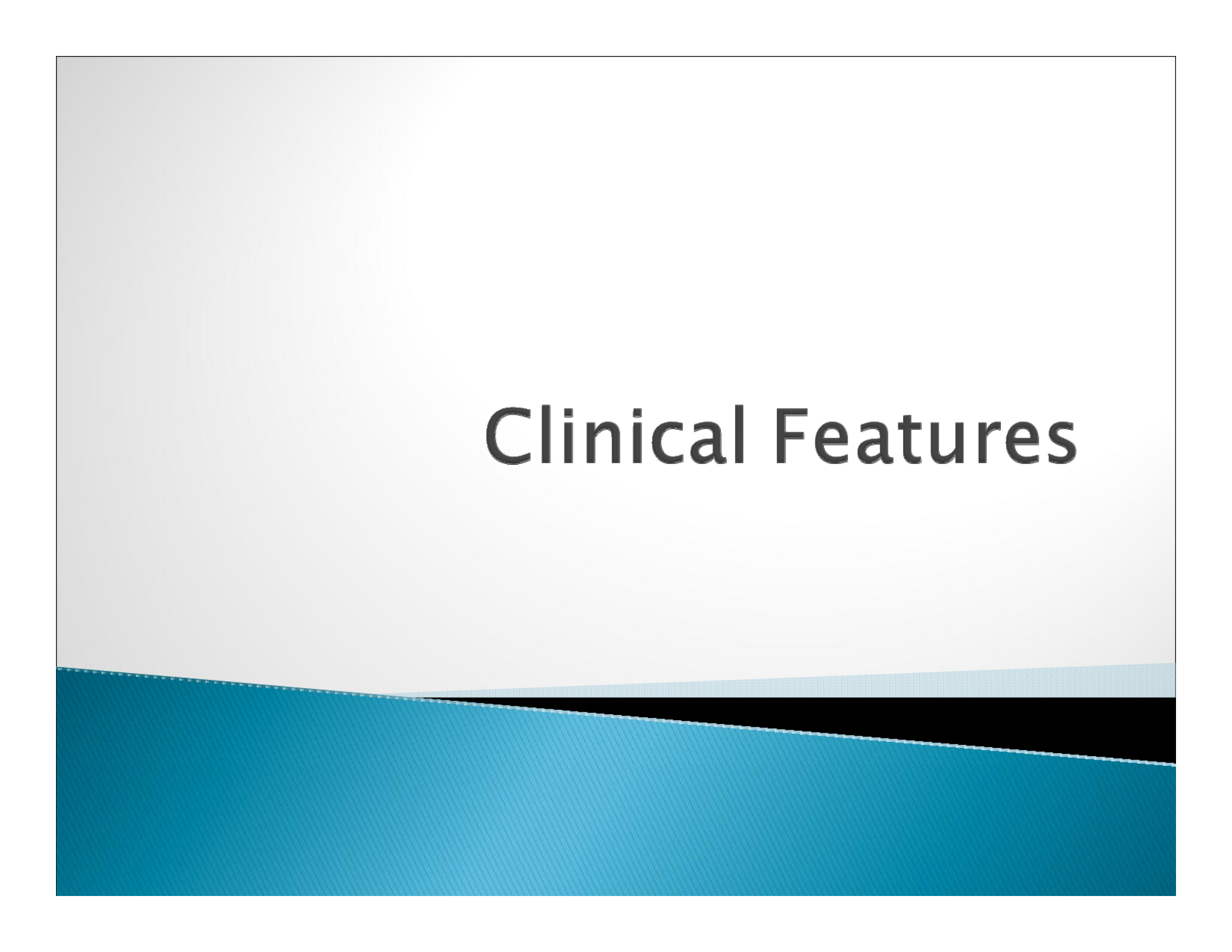


Centre for Health Protection

Department of Health

The Government of the Hong Kong Special Administrative Region

Clinical Features

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Tetanus – Clinical Features

- ▶ incubation period
 - 3 to 21 days (varies from 2 to 60 days)
 - 90% present within 15 days
- ▶ neonatal tetanus
 - 4 to 14 days after birth, averaging about 7 days
- ▶ incubation period & period of onset
 - in relation with injury site from the CNS
 - prognostic importance
 - shorter times – more severe disease & higher mortality

Tetanus – Clinical Features

- ▶ almost all reported cases
 - never been vaccinated or
 - completed primary series but not had booster in the preceding 10 years
- ▶ presenting symptoms – pain & stiffness
 - Alfery DD, Rauscher A. Tetanus: a review. Crit Care Med 1979; 4: 176–81
- ▶ 4 different forms
 1. local tetanus
 2. cephalic tetanus
 3. generalized tetanus
 4. neonatal tetanus

Local Tetanus

- ▶ uncommon
- ▶ maybe the result of immunization
- ▶ confined to a limb or muscle
 - in close proximity to site of injury
- ▶ persist for weeks
- ▶ may precede the onset of generalized tetanus
 - generally milder
- ▶ mortality – about 1%

Cephalic Tetanus

- ▶ rare
- ▶ occasionally occur with otitis media
 - *C. tetani* – flora of the middle ear
- ▶ follows eye infection or head injury
- ▶ characterized by variant cranial nerves palsies
 - CN VII – most common
- ▶ Ophthalmoplegic Tetanus
 - CN II palsies & ptosis
- ▶ progression to generalized form – common
- ▶ high mortality



Left facial nerve palsy and recent scar in patient with cephalic tetanus
(Dr T. M. Cook, taken at the University of Oxford Clinical Research
Unit, Centre for Tropical Diseases, Ho Chi Minh City, Viet Nam)

Generalized Tetanus

- ▶ most common (~80%)
- ▶ present with a descending pattern
 - trismus or lockjaw
 - present in 75% of cases – first sign
 - risus sardonicus (clenched-teeth expression)
 - stiffness of the neck
 - dysphagia
 - muscle rigidity

Generalized Tetanus

- ▶ typical spasms
 - flexion & adduction of arms
 - extension of legs
 - opisthotonos
 - painful
 - fractures, dislocation & tendon separations
- ▶ external stimuli e.g. noise, light or touch
- ▶ life-threatening
 - larynx and / or diaphragm involvement



Photo Courtesy of the Centers for Disease Control

Photo Courtesy of the Centers for Disease Control



Photo Courtesy of the Centers for Disease Control

Neonatal Tetanus

- ▶ a form of generalized tetanus – newborn infants
- ▶ through infection of unhealed umbilical stump
 - without protective passive immunity
- ▶ typical spasms
 - misdiagnosed as convulsion of other etiologies



Severe spasm with flexion of the arms in tetanus neonatorum
(Dr J. Farrar and Dr C. Parry of the University of Oxford Clinical
Research Unit, Centre for Tropical Diseases, Ho Chi Minh City,
Viet Nam)



Severe opisthotonos in tetanus neonatorum
(Dr J. Farrar and Dr C. Parry of the University of Oxford Clinical
Research Unit, Centre for Tropical Diseases, Ho Chi Minh City,
Viet Nam)

Autonomic Dysfunction

- ▶ occurs in severe cases

- Alfery DD, Rauscher LA. Tetanus: a review. *Crit Care Med* 1979; 7: 176–81
- Kerr JH, Corbett JL, Prys-Roberts C *et al.* Involvement of the sympathetic nervous system in tetanus. *Lancet* 1968; 2: 236–41
- Tsueda K, Oliver PB, Richter RW. Cardiovascular manifestations of tetanus. *Anesthesiology* 1974; 40: 588–92

- ▶ begins a few days after muscle spasms
 - toxin reaches lateral horns of spinal cord

- ▶ increased basal sympathetic tone
 - tachycardia
 - bowel & bladder dysfunction

Autonomic Dysfunction

- ▶ episodes of sympathetic over-activity – both α - and β -receptors
 - increase in vascular resistance, central venous pressure & cardiac output (usually)
- ▶ manifestations:
 - labile hypertension
 - pyrexia
 - sweating
 - pallor
 - cyanosis of digits
- ▶ usually short duration
- ▶ occur without provocation

Autonomic Dysfunction

- ▶ reduced inhibition of post-synaptic sympathetic fibres in the intermediolateral cell column
 - high circulating catecholamine concentration
- ▶ other postulated mechanisms:
 - loss of inhibition of adrenal medulla
 - direct inhibition of the release of endogenous opiates by tetanospasmin
 - increased release of thyroid hormone

Autonomic Dysfunction

- ▶ role of parasympathetic nervous system – unclear
 - episodes of bradycardia
 - low peripheral vascular resistance
 - low central venous pressure
 - profound hypotension
- ▶ frequently pre-terminal

- ▶ sudden & repeated cardiac arrest
 - total withdrawal of sympathetic tone
 - Kerr J. Current topics in tetanus. *Intens Care Med* 1979; 5: 105-10
 - catecholamine-induced myocardial damage
 - direct brainstem damage

Tetanic Seizure

- ▶ poor prognosis
- ▶ frequency & severity of seizure
 - related to severity of the disease
- ▶ resemble epileptic seizure – sudden burst of tonic contractions
- ▶ NO loss of consciousness

Differential Diagnosis

- ▶ local oral / temporomandibular disease
- ▶ hypocalcaemic tetany
- ▶ convulsion
- ▶ dystonic reaction to drugs
- ▶ Strychnine poisoning
- ▶ psychiatric disorders

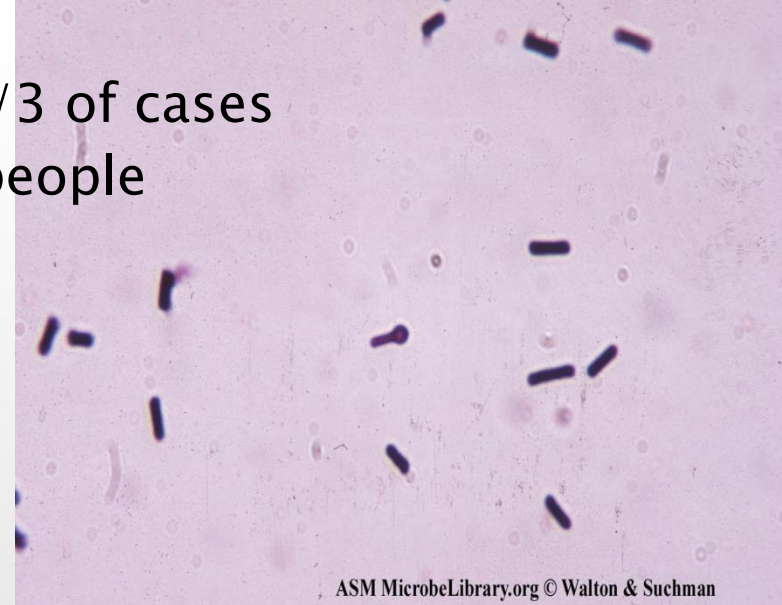


Diagnosis

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Diagnosis

- ▶ clinical
 - NOT depends on bacteriologic confirmation
- ▶ NO laboratory test specific to tetanus
- ▶ *C. tetani*
 - cultured from the wound in 1/3 of cases
 - can be isolated from normal people



ASM MicrobeLibrary.org © Walton & Suchman

Severity

- ▶ several grading systems are reported

Table 1 Prognostic scoring systems in tetanus: Dakar score

<i>Prognostic factor</i>	<i>Dakar score</i>	
	<i>Score 1</i>	<i>Score 0</i>
Incubation period	<7 days	≥7 days or unknown
Period of onset	<2 days	≥2 days
Entry site	Umbilicus, burn, uterine, open fracture, surgical wound, intramuscular injection	All others plus unknown
Spasms	Present	Absent
Fever	>38.4°C	<38.4°C
Tachycardia	Adult>120 beats/min Neonate>150 beats/min	Adult<120 beats/min Neonate<150 beats/min
Total score		

JJ Farrar, LM Yen, T Cook, *et al.* Tetanus. *J Neurol Neurosurg Psychiatry* 2000; 69: 292–301

Severity

Table 2 Prognostic scoring systems in tetanus: Phillips score

Factor	Score
Incubation time:	
<48 hours	5
2–5 days	4
5–10 days	3
10–14 days	2
>14 days	1
Site of infection:	
Internal and umbilical	5
Head, neck, and body wall	4
Peripheral proximal	3
Peripheral distal	2
Unknown	1
State of protection:	
None	10
Possibly some or maternal immunisation in neonatal patients	8
Protected >10 years ago	4
Protected <10 years ago	2
Complete protection	0
Complicating factors:	
Injury or life threatening illness	10
Severe injury or illness not immediately life threatening	8
Injury or non-life threatening illness	4
Minor injury or illness	2
ASA Grade 1	0
Total score	

Table 4 New prognostic score: Tetanus Severity Score (TSS). The final score is calculated from the total of individual section scores

	Score
Age (year)	
≤70	0
71–80	5
>80	10
Time from first symptom to admission (days)	
≤2	0
3–5	–5
>5	–6
Difficulty breathing on admission	
No	0
Yes	4
Co-existing medical conditions*	
Fit and well	0
Minor illness or injury	3
Moderately severe illness	5
Severe illness not immediately life threatening	5
Immediately life-threatening illness	9
Entry site†	
Internal or injection	7
Other (including unknown)	0
Highest systolic blood pressure recorded during first day in hospital (mmHg)	
≤130	0
131–140	2
>140	4
Highest heart rate recorded during first day in hospital (bpm)	
≤100	0
101–110	1
111–120	2
>120	4
Lowest heart rate recorded during first day in hospital (bpm)	
≤110	0
>110	–2
Highest temperature recorded during first day in hospital (°C)	
≤38.5	0
38.6–39	4
39.1–40	6
>40	8

CL Thwaites *et al.* Predicting the clinical outcome of tetanus: the tetanus severity score. *Tropical Medicine and International Health* Mar 2006; 11(3): 279–87

Ablett Classification of the Severity of Tetanus²¹

Grade		Clinical Features
I	Mild	Mild to moderate trismus; general spasticity; no respiratory embarrassment; no spasms; little or no dysphagia
II	Moderate	Moderate trismus; well-marked rigidity; mild to moderate but short spasms; moderate respiratory embarrassment with an increased respiratory rate greater than 30, mild dysphagia
III	Severe	Severe trismus; generalized spasticity; reflex prolonged spasms; respiratory rate greater than 40; apnoeic spells, severe dysphagia; tachycardia > 120.
IV	Very severe	Grade III and violent autonomic disturbances involving the cardiovascular system. Severe hypertension and tachycardia alternating with relative hypotension and bradycardia, either of which may be persistent.

Ablett J.J.L. Analysis and main experiences in 82 patients treated in the Leeds Tetanus Unit. In: Ellis M, ed. *Symposium on Tetanus in Great Britain*. Boston Spa, UK: National Lending Library, 1967; 1-10

Management

The background of the slide is a light gray gradient. At the bottom, there is a dark blue wavy shape that resembles a stylized landscape or water. A thin black horizontal line separates the blue shape from the gray background.

Management – Objectives

1. to **eradicate** the source of toxin
 - hygiene, surgery & antibiotic
2. to **prevent** toxin from entering peripheral nerves
 - wound care
3. to **neutralize** circulating toxin
 - passive immunization
4. to **minimize** the effect of toxin

Wound Care

- ▶ to eradicate the toxin

- wounds should be cleaned +/- surgical debrided

- Edmondson RS, Flowers MW. Intensive care in tetanus: management, complications and mortality in 100 cases. *BMJ* 1979; 1: 1401-4
- Groleau G. Tetanus. *Emerg Med Clin N Am* 1992; 10: 351-60

- removal of foreign materials

- extensive debridement of necrotic tissue

Antibiotics

- ▶ spores can be destroyed by antibiotics
- ▶ vegetative form (bacillus) – sensitive to antibiotic in vitro
 - antibiotic concentration at wound site
- ▶ **Penicillin G** (1–3MU IV 6 hourly for 10 days)
 - GABA antagonist
 - Johnson HC, Walker A. Intraventricular penicillin. *JAMA* 1945; **127**: 217–9
- ▶ **Metronidazole** (500mg IV 8–hourly for 10 days)
 - at least as good result as Penicillin
 - Ahmadsyah I, Salim A. Treatment of tetanus: an open study to compare the efficacy of procaine penicillin and metronidazole. *BMJ* 1985; **291**: 648–50
 - Yen LM, Dao LM, Day NPJ, *et al.* Management of tetanus: a comparison of penicillin and metronidazole. *Symposium of antimicrobial resistance in southern Viet Nam*. 1997
 - more effective than Penicillin

Antibiotics

- ▶ alternative choices:
 - Erythromycin
 - Tetracycline
 - Chloramphenicol
 - Clindamycin

Passive Immunization

- ▶ human tetanus immune globulin (3000 – 6000units im)
 - neutralize circulating toxin
 - NOT affect toxin fixed in the CNS
 - not ameliorate symptom
 - replace anti-tetanus serum (of horse origin)
- ▶ NO controlled study –
 - ▶ shown to be more effective than wound toilet & Penicillin administration
 - Abrutyn E. Tetanus. In: Isselbacher KJ, Wilson J, Fauci A, *et al.*, eds. *Harrison's Principles of Internal Medicine* 13th edn. New York: McGraw-Hill Inc, 1995; 633–5
 - Alfery DD, Rauscher A. Tetanus: a review. *Crit Care Med* 1979; 4: 176–81
 - Groleau G. Tetanus. *Emerg Med Clin N Am* 1992; 10: 351–60

Passive Immunization

▶ Intrathecal anti-tetanus toxin

- reported to be ineffective

- Abrutyn E, Berlin JA. Intrathecal therapy in tetanus: a meta-analysis. *JAMA* 1991; 266: 2262-7

- showed better clinical progression

- Miranda-Filho Dde B, Ximenes RA, Barone AA *et al.* Randomised controlled trial of tetanus treatment with antitetanus immunoglobulin by the intrathecal or intramuscular route. *Br Med J* 2004; 328: 615-17

▶ still controversial

▶ suitable intrathecal preparation – not widely available

Passive Immunization

- ▶ side effects
 - fever
 - shivering
 - chest or back pain
 - tachycardia
 - hypotension
- ▶ intravenous immune globulin (IVIG)
 - contain tetanus anti-toxin maybe used if anti-tetanus toxin not available

Management of Muscle Spasm

- ▶ **endotracheal intubation or tracheostomy**
 - at risk of laryngeal spasm
- ▶ **mechanical ventilation**
- ▶ **avoidance of unnecessary stimulation**
- ▶ **mainstay of treatment is sedation**
 - prevent muscle spasm
 - improve autonomic dysfunction

Controlling Muscle Spasm

- ▶ **Benzodiazepines** – augment GABA agonism

- ▶ **Diazepam**

- long acting metabolites

- Lipman J, James MFM, Erskine J, Plit ML, Eidelman J, Esser JD. Autonomic dysfunction in severe tetanus: magnesium sulfate as an adjunct to deep sedation. *Crit Care Med* 1987; 15: 987-8

- ▶ **Midazolam**

- less apparent cumulation

- Gyasi HK, Fahr J, Kurian E, Mathew M. Midazolam for prolonged intravenous sedation in patients with tetanus. *Mid EJ Anesth* 1993; 12: 135-41

- ▶ **Propofol**

- control of spasms & rigidity without the use of neuromuscular blocking drugs

- Borgeat A, Popovic V, Schwander D. Efficiency of a continuous infusion of propofol in a patient with tetanus. *Crit Care Med* 1991; 19: 295-7
 - Peduto VA, Pisanu GM, Piga M. Midazolam, propofol, and clonidine for sedation and control of autonomic dysfunction in severe generalised tetanus. *Minerv Anesth* 1993; 59: 171-8

Controlling Muscle Spasm

- ▶ additional sedation – anticonvulsants
 - Phenobarbitone
 - Phenothiazines (usually Chlorpromazine)
- ▶ muscle relaxants
 - to allow effective ventilation
 - any muscle relaxant – long acting agents preferred
- ▶ **Pancuronium** – worsen autonomic instability reported
 - Buchanan N, Cane RD, Wolfson G, De Andrade M. Autonomic dysfunction in tetanus: the effects of a variety of therapeutic agents, with special reference to morphine. *Intensive Care Med* 1979; 5: 65–8
 - Spelman D, Newton–John H. Continuous pancuronium infusion in severe tetanus. *Med J Aust* 1980; 1: 676
- ▶ **Vecuronium**
 - Powles AB, Ganta R. Use of vecuronium in the management of tetanus. *Anaesthesia* 1985; 40: 879–81
- ▶ **Atracurium**
 - Peat SJ, Potter DR, Hunter JM. The prolonged use of atracurium in a patient with tetanus. *Anaesthesia* 1988; 43: 962–3
- ▶ **Pipecuronium & Rocuronium**

Controlling Muscle Spasm

▶ Dantrolene

- Tidyman M, Prichard JG, Deamer RL, Mac N. Adjunctive use of dantrolene in severe tetanus. *Anesth Analg* 1985; **64**: 538-40

▶ Intrathecal Baclofen – GABA_B agonist

- 500 – 2000 µg/day
- significant number developed coma & respiratory depression
 - Dressnandt J, Konstanzer A, Weinzierl FX, Pfab R, Klingelhöfer J. Intrathecal baclofen in tetanus: four cases and a review of reported cases. *Intensive Care Med* 1997; **23**: 896-902
 - Saissy JM, Demaziere J, Vitris M, *et al.* Treatment of severe tetanus by intrathecal injections of baclofen without artificial ventilation. *Intensive Care Med* 1992; **18**: 241-4

Management of Autonomic Dysfunction

- ▶ sedation – to decrease catecholamine output

- ▶ **Benzodiazepine**

- increase the affinity & efficacy of GABA

- ▶ **Morphine**

- acts by replacing deficient endogenous opioids
 - without cardiac compromise

- Rie MA, Wilson RS. Morphine therapy controls autonomic hyperactivity in tetanus. *Ann Inter Med* 1978; **88**: 653-4
 - Rocke DA, Wesley AG, Pather M, Calver AD, Hariparsad D. Morphine in tetanus – the management of sympathetic nervous system overactivity. *S Afr Med J* 1986; **70**: 666-8

- ▶ **very large doses may be required**

- Diazepam – 3400mg/day
 - Morphine – 235mg/day

Management of Autonomic Dysfunction

- ▶ combination of α - and β -adrenergic blockers – traditional approach
- ▶ α -receptor blockers
 - Phenoxybenzamine
 - Phentolamine
 - Bethanidine
 - Chlorpromazine
 - Prys-Roberts C, Kerr JH, Corbett JL, Crampton Smith A, Spalding JM. Treatment of sympathetic overactivity in tetanus. *Lancet* 1969; i: 542–6
- ▶ unopposed β -adrenergic blockade – NOT advised
 - deaths from acute congestive cardiac failure
 - Buchanan N, Smit L, Cane RD *et al.* Sympathetic overactivity in tetanus: fatality associated with propranolol. *Br Med J* 1978; 2: 254–5
 - Wesley AG, Hariparsad D, Pather M *et al.* Labetalol in tetanus. *Anaesthesia* 1983; 38: 243–9
- ▶ Esmolol
 - to control sympathetic crises
 - King WW, Cave DR. Use of esmolol to control autonomic instability of tetanus. *Am J Med* 1991; 91: 425–8

Management of Autonomic Dysfunction

▶ Magnesium Sulphate

- pre- synaptic neuromuscular blocker
- used as an adjunct to sedation
 - Lipman J, James MFM, Erskine J *et al.* Autonomic dysfunction in severe tetanus: magnesium sulphate as an adjunct to deep sedation. *Crit Care Med* 1987; 15: 987-8
 - James MFM, Manson EDM. The use of magnesium sulphate infusions in the management of very severe tetanus. *Intens Care Med* 1985; 11: 5-12
- decreased systemic vascular resistance, pulse rate & small decrease in cardiac output
- reduce the intensity of muscle spasm
- aim for concentration 2.5-4.0mmol/L
- calcium supplement

▶ NOT shown to decrease the need of mechanical ventilation

- Thwaites CL, Yen LM, Loan HT *et al.* Magnesium sulphate for treatment of severe tetanus: a randomised controlled trial. *Lancet* 2006; 368: 1436-43
- Mathew PJ, Samra T, Wig J. Magnesium sulphate for treatment of tetanus in adults. *Anaesthesia & Intensive Care* 2010 Jan; 38(1): 185-9

▶ inadequate in controlling symptoms alone

Management of Autonomic Dysfunction

▶ Clonidine

- central α_2 -agonist
- produce sedation with control of autonomic dysfunction
 - Sutton DN, Tremlett MR, Woodcock TE, Nielsen MS. Management of autonomic dysfunction in severe tetanus: the use of magnesium sulphate and clonidine. *Intensive Care Med* 1990; 16: 75–80
- no alteration in haemodynamic instability
 - Brown JL, Sinding H, Mathias CJ. Autonomic disturbance in severe tetanus: failure of parenteral clonidine to control blood pressure. *J Infect* 1994; 29: 67–71

▶ Atropine

- dose up 100mg/hr were used
- autonomic block , central sedation +/- neuromuscular block
 - Dolar D. The use of continuous atropine infusion in the management of tetanus. *Intensive Care Med* 1992; 18: 26–31

Management of Autonomic Dysfunction

▶ Dexmedetomidine

- potent selective α_2 agonist
- may also have an effect in reducing sympathetic overactivity
 - N. K. Girgin, R. Iscimen, A. Gurbet, F. Kahveci, and O. Kutlay. Dexmedetomidine sedation for the treatment of tetanus in the intensive care unit. *Br. J. Anaesth.*, Oct, 2007; 99(4): 599 – 600
- potent use in the future?

▶ Sodium valproate

- blocks GABA–aminotransferase
- prevent clinical effect of tetanus toxin in animal studies
 - Foca A, Rotiroti D, Mastroeni P, Nistico G. Effects of tetanus toxin after intracerebral microinjection are antagonised by drugs enhancing GABAergic transmission in adult fowl. *Neuropharmacology* 1984; 23: 155–8

Supportive Treatment

- ▶ nutrition
- ▶ measures to prevent
 - contractures
 - nosocomial pneumonia
 - Udwadia FE. Pulmonary function in tetanus. In: Udwadia FE, ed., *Tetanus*. New York: Oxford University Press, 1994
 - deep-vein thrombosis
- ▶ active immunization
- ▶ psychological support

Complications



Complications

Table 2 Complications of tetanus. Life-threatening complications are indicated by an asterisk (*)

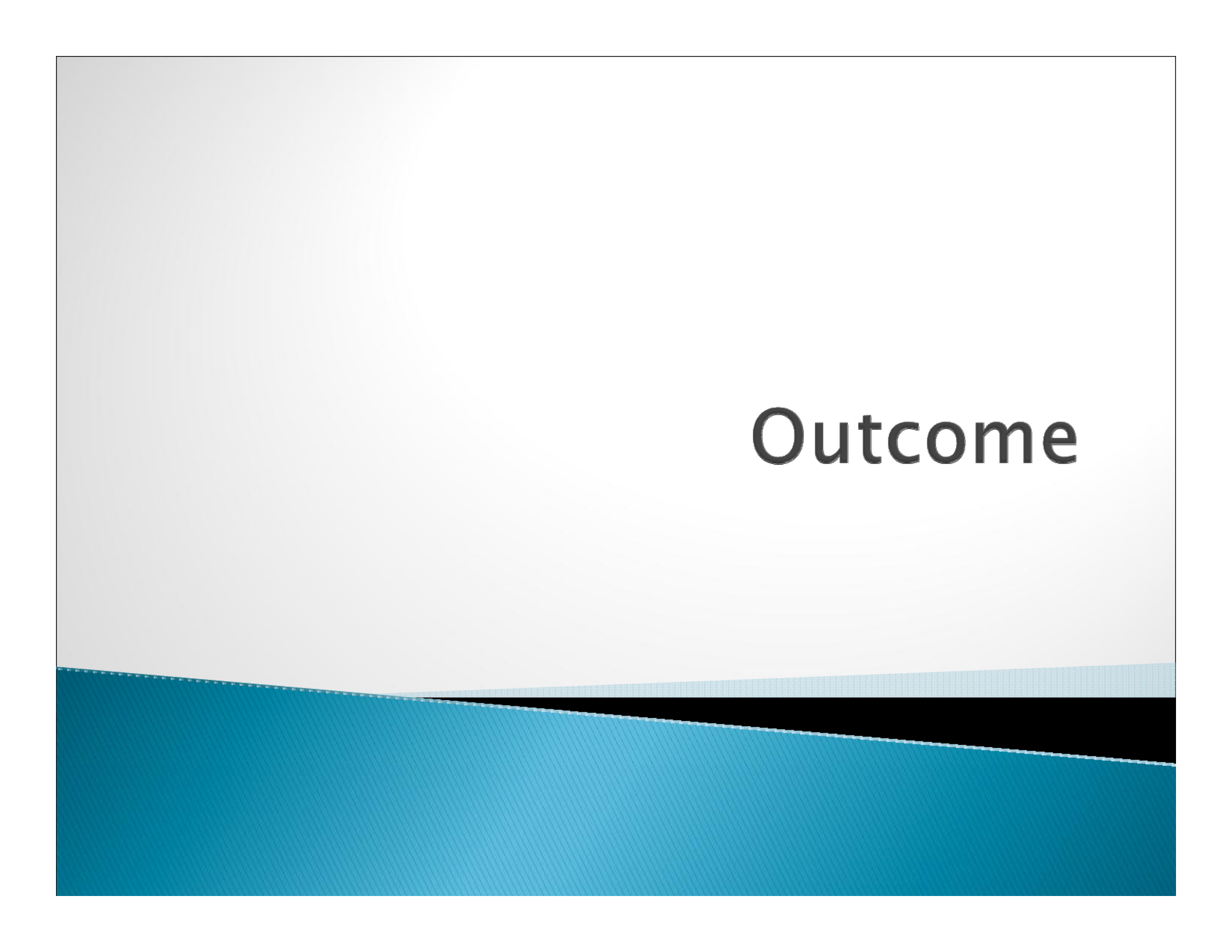
Body system	Complication
Airway	Aspiration* Laryngospasm/obstruction* Sedative associated obstruction*
Respiratory	Apnoea* Hypoxia* Type I* (atelectasis, aspiration, pneumonia) and type II* respiratory failure (laryngeal spasm, prolonged truncal spasm, excessive sedation) ARDS* Complications of prolonged assisted ventilation (e.g. pneumonia) Tracheostomy complications (e.g. tracheal stenosis)
Cardiovascular	Tachycardia*, hypertension*, ischaemia* Hypotension*, bradycardia* Tachyarrhythmias, bradyarrhythmias* Asystole* Cardiac failure*
Renal	High output renal failure* Oliguric renal failure* Urinary stasis and infection
Gastro-intestinal	Gastric stasis Ileus Diarrhoea
Miscellaneous	Haemorrhage* Weight loss* Thromboembolus* Sepsis and multiple organ failure* Fractures of vertebrae during spasms Tendon avulsions during spasms

Cook TM, R.T.Protheroe, J.M.Handel.
Tetanus: a review of the literature.
British Journal of Anaesthesia 2001;
87:477-87

Complications

- ▶ **cardiovascular complications**
 - cardiac failure, arrhythmias, pulmonary edema & hypertensive crises
- ▶ **hypoxia**
 - laryngospasm and/or spasm of respiratory muscles
- ▶ **aspiration pneumonia**
- ▶ **complications of mechanical ventilation**
- ▶ **fractures**
 - especially of mid-thoracic vertebrae
- ▶ **myoglobinuria**
- ▶ **fluid & electrolyte disturbance**
- ▶ **nosocomial infections**
- ▶ **deep-vein thrombosis & pulmonary embolism**

- ▶ **NO obvious pathology identified – 20% of tetanus deaths**



Outcome

Outcome & Prognosis

▶ mortality rate – varies

- neonates in African countries
 - 80% with no ICU facilities
 - 10% with artificial ventilation
- non-neonates in the United State
 - 0% under 30 years
 - 50% for 60 years or older

• reported reduction in mortality from 44 to 15% after the introduction of intensive care treatment

- Trujillo MH, Castillo A, Espana J, Manzo A, Zerpa R. Impact of intensive care management on the prognosis of tetanus. Analysis of 641 cases. *Chest* 1987; **92**: 63-5

▶ cases most likely to be fatal

- 60 years of age or older (18%)
- unvaccinated group (22%)
- diabetes (31%)

Outcome & Prognosis

- ▶ other poor prognostic factors:
 - short incubation period
 - early onset of convulsions
 - delay in treatment
 - contaminated lesions of face & head
 - neonatal tetanus

Outcome & Prognosis

- ▶ severe cases require ICU admission

- approximately 3–5 weeks

- Reis E, Freire E, Alexandrino S. Tetanus in an ICU in Portugal. Epidemiology, incubation and complications. *Int J Intensive Care* 1994; 1: 120–21
 - Trujillo MH, Castillo A, Espana J, Manzo A, Zerpa R. Impact of intensive care management on the prognosis of tetanus. Analysis of 641 cases. *Chest* 1987; 92: 63–5
 - Udwadia FE. Haemodynamics in severe in tetanus. In: Udwadia FE, ed., *Tetanus*. New York: Oxford University Press, 1994

- ▶ the average mortality rate for most ICUs – 10–11%

- Sanford JP. Tetanus – forgotten but not gone. *N Engl J Med* 1995; 332: 812–3

Outcome & Prognosis

- ▶ muscle spasm disappear after 1–3 weeks
 - most survivors recover by 6 weeks

- ▶ recovery – thought to be complete
 - reported cases of abnormal neurological features
 - intellectual or emotional changes
 - fits / myoclonic jerks
 - sleep disturbance
 - decrease libido
 - resolved within 2 years
 - Illis LS, Taylor FM. Neurological and electroencephalographic sequelae of tetanus. *Lancet* 1971; i: 826–30

Prevention



Prevention – Immunization

- ▶ **completely preventable** by active immunization
- ▶ **almost all reported cases**
 - never been vaccinated
 - completed a primary series but not had a booster in the preceding 10 years
- ▶ **Tetanus Toxoid** – formaldehyde-treated toxin
 - first produced in 1924
 - protective level – 0.1IU/ml
- ▶ **2 types of toxoid**
 - adsorbed toxoid (aluminum salt precipitated)
 - fluid toxoid
- ▶ **usually in form of diphtheria, tetanus, and acellular pertussis vaccine (DTP) for children**
 - ▶ **routine boosters recommended every 10 years**

MAN DIES FROM SCRATCH

It's only a scratch

Three days after making this statement, Mr Roger Smith began to suffer from muscular convulsions and facial spasms.

Six days later, he was pronounced dead at Royal Free Hospital, London. The cause of death was tetanus.

TIN OPENER

At the inquest, Mrs. Smith stated that her husband had been opening a tin of peas, when the opener slipped, producing a slight cut along the inside of the thumb and palm. Rather than cleansing the wound immediately, Mr. Smith had continued working in the kitchen, and then in the garden.

The coroner's verdict was heart failure, brought on by poisonous tetanus spores which had gained access through the scratch on Mr. Smith's hand. Mr. Smith was 34.



It happens every week: Doctor

At a meeting of the BMA, Dr. Alvin Johnson said that tetanus could be completely prevented by a course of three injections, over a period of twelve months, followed by a booster every five years. These could easily be administered by a local doctor.

"Most tetanus cases are caused by simple scratches or cuts, which are allowed to become infected. It happens every week at work, or around the house."

Dr. Johnson also warned that even small cuts should be treated immediately. Anyone attending a hospital with a skin injury should expect a course of anti-tetanus injections.

"Once tetanus is established in a patient we are virtually powerless. Over 50% of severe established cases result in death. Immunisation is essential, and should be considered common practice for adults and children alike."

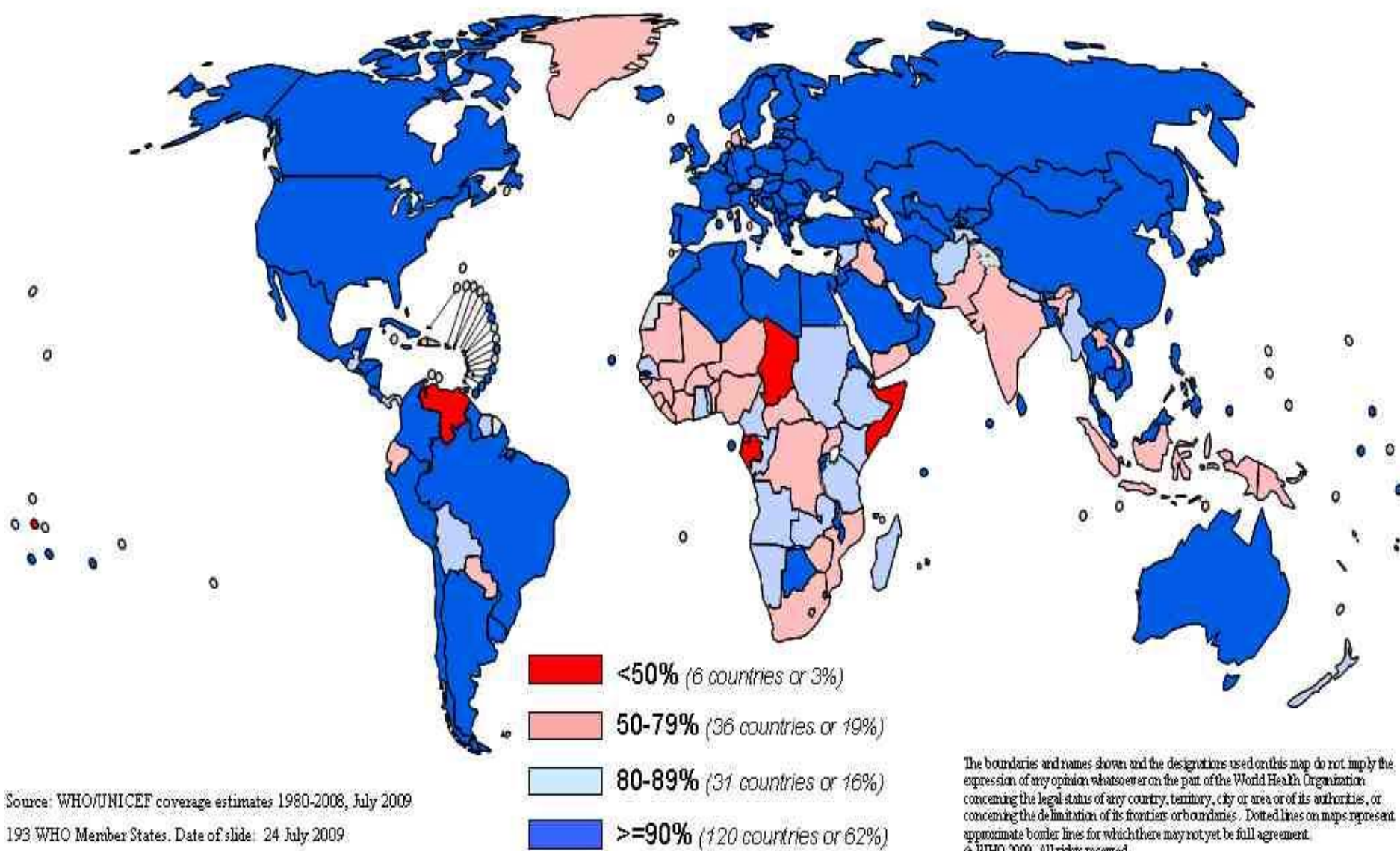
A course of anti-tetanus injections could save your life

The longer you put it off, the more chance there is of a cut or scratch becoming dangerously infected.

The Health Education Council 

Poster informing the public about tetanus, United Kingdom, 1969-1987

Immunization coverage with DTP3 vaccines in infants, 2008



Prevention – Wound Management

- ▶ antibiotic prophylaxis – neither practical nor useful
- ▶ **active immunization +/– passive immunization**
 - condition of the wound
 - patient's immunization history

Prevention – Wound Management

Summary Guide to Tetanus Prophylaxis in Wound Management

History of tetanus immunization (doses)	Clean, minor wounds		All other wounds ¹	
	Td ²	TIG ³	Td	TIG ³
Uncertain or <3	Yes ⁴	No	Yes ⁴	Yes
3 or more	No ⁵	No	No ⁶	No

ICU Day 1

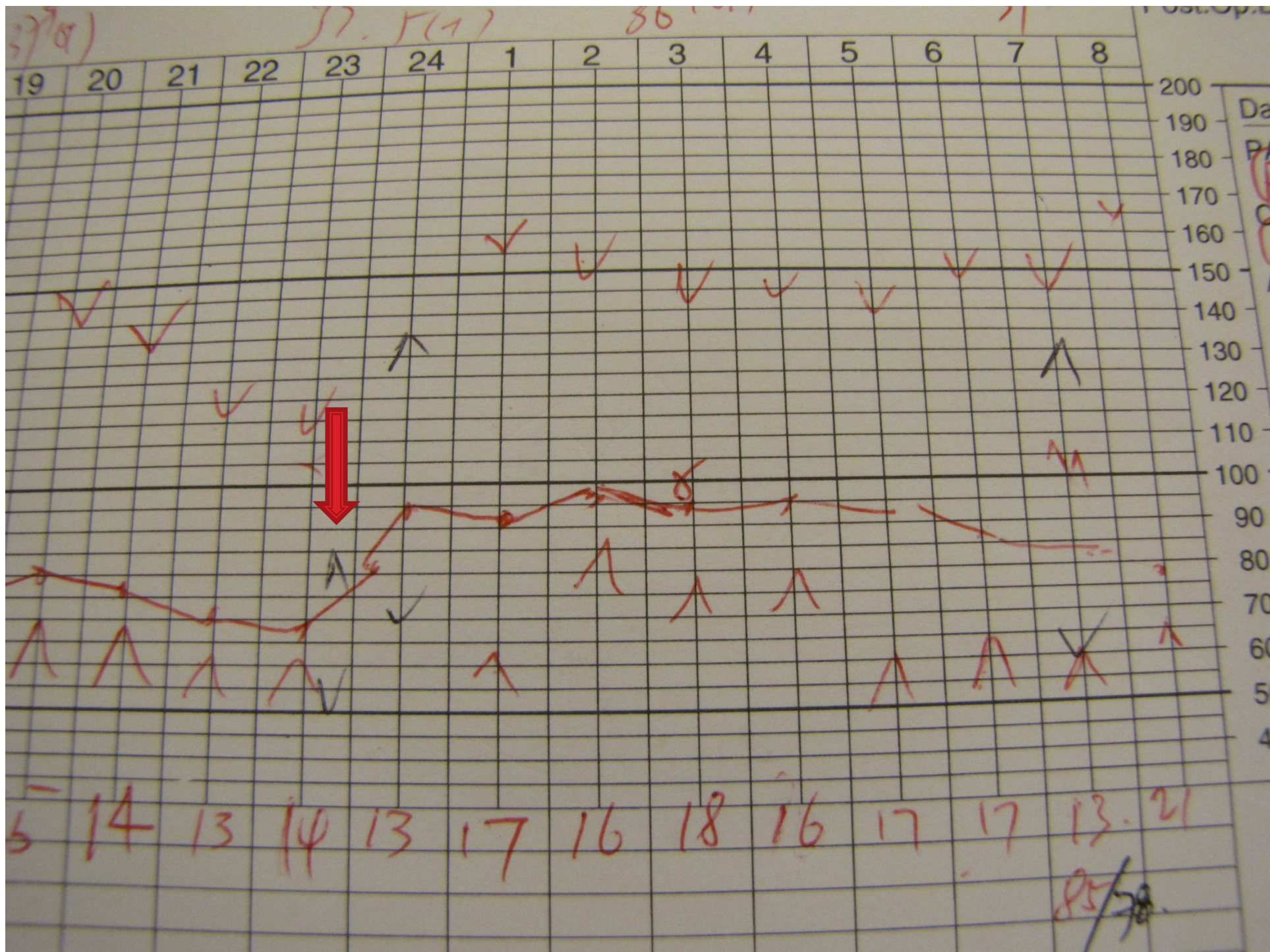
- ▶ septic workup
- ▶ Penicillin G 3MU Q4H → 4MU Q4H (Day 2)
- ▶ Flagyl 500mg Q8H
- ▶ Anti-tetanus immunoglobulin 3000IU (intra-muscular)
- ▶ Tetanus Toxoid 0.5ml (Intra-muscular)
- ▶ Midazolam & Morphine infusion

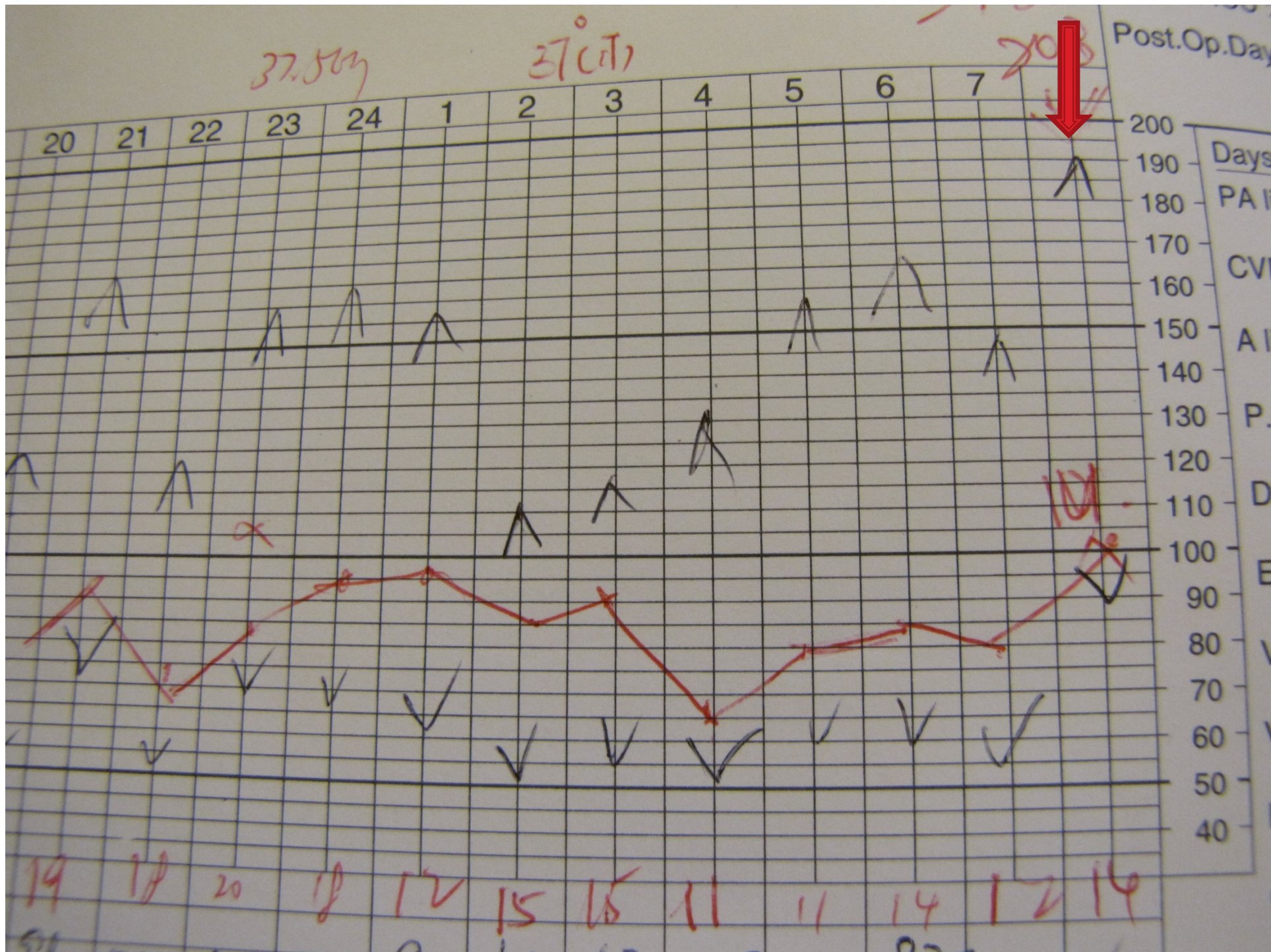
ICU Day 1

- ▶ surgical team consulted for ? need for debridement
 - clean base scalp wound
 - for daily wound dressing
 - for 2^o suturing later
- ▶ wound swab (5th Jan, 2009)
 - Staphylococcus aureus

ICU Progress

- ▶ episodes of hypotension (BP: 76/47mmHg)
 - fluid resuscitation given
 - low dose Adrenaline infusion started
- ▶ Bedside Echocardiogram:
 - mild decrease EF globally 50–55%
 - no definite RWMA
 - normal MV & AV with mild MR & AR





ICU Progress

- ▶ surgical tracheostomy performed on Day 6
- ▶ pneumatic sequential compression & LMWH
 - DVT prophylaxis





ICU Progress

- ▶ nosocomial infection
 - TA: Staphylococcus aureus
 - urine: E. Coli
- ▶ slow weaning course
 - mechanical ventilation weaned on 26th Jan, 2009 (Day 22)
- ▶ neck hyper-extension slowly resolved
- ▶ discharged to general ward on 28th Jan, 2009

Rehabilitation

- ▶ ENT consulted –
 - adequate glottic airway
 - tracheotomy subsequent weaned

- ▶ transferred to Kowloon Hospital for rehabilitation
 - course of physical & ADL training given
 - satisfactory functional control over 4 limbs
 - walking tolerance up to 200 meters with stick
 - independent in basic ADL

- ▶ discharged home on 7th Apr, 2009

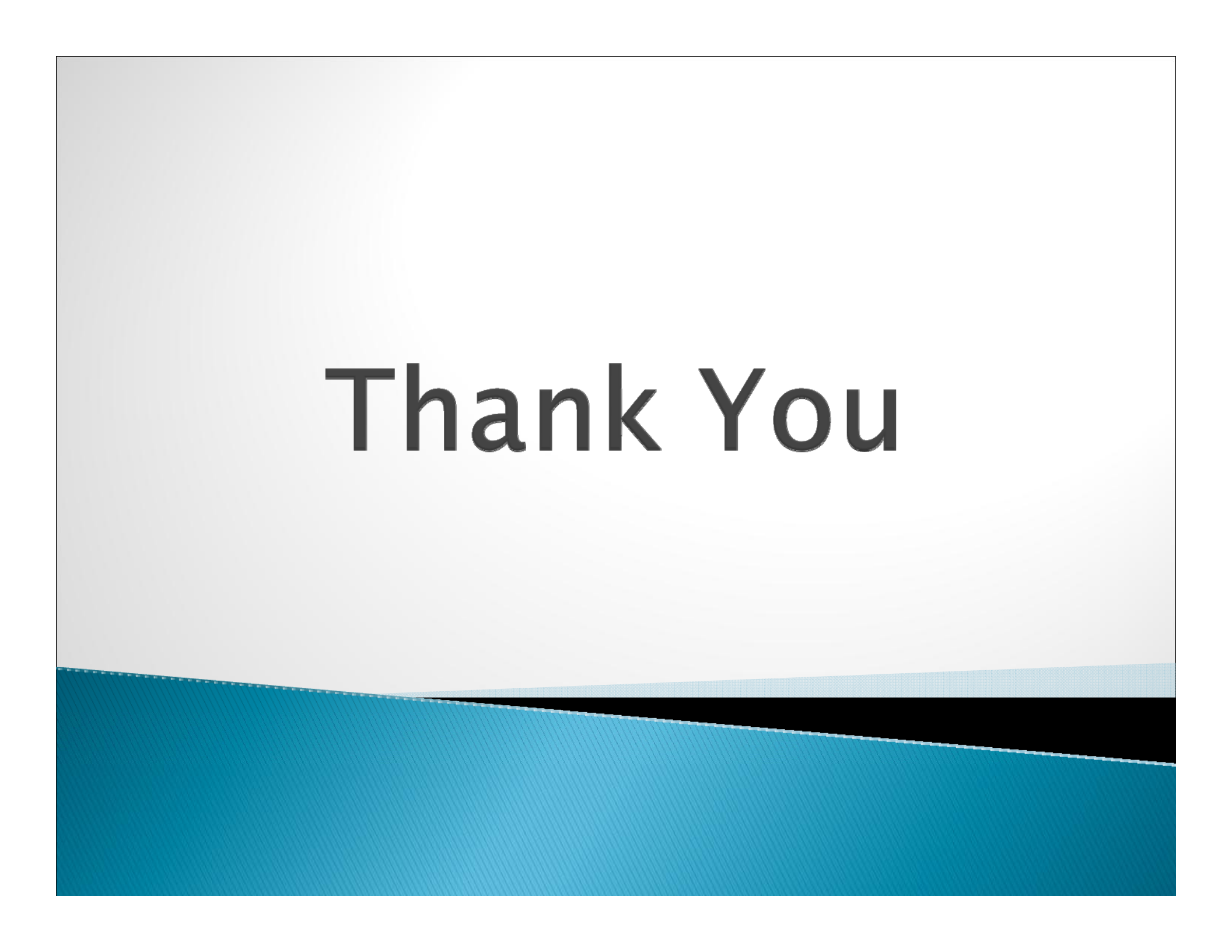
Conclusions – Tetanus

- ▶ rare disease in Hong Kong
- ▶ entirely preventable by vaccination
- ▶ remains a health problem world-wide
 - mainly in the elderly & unimmunized population in developed area
- ▶ diagnosis is mainly clinical
- ▶ mortality remains high
- ▶ prolonged intensive care support maybe necessary

Conclusions – Tetanus

- ▶ most treatment is based on **limited evidence**
- ▶ major therapeutic challenges
 - control of muscular rigidity & spasms
 - treatment of autonomic disturbance
 - prevention of complications associated with **prolonged critical illness**
- ▶ return to **normal function** can be expected

Thank You

The background of the slide is a light gray gradient. At the bottom, there is a dark blue wavy shape that resembles a stylized landscape or water. A thin black horizontal line separates the blue shape from the gray background.