

ZOÖNOSES



STEVEN VAN DEN BROUCKE

NAJAARSYMPOSIUM KARVA 27-11-2021

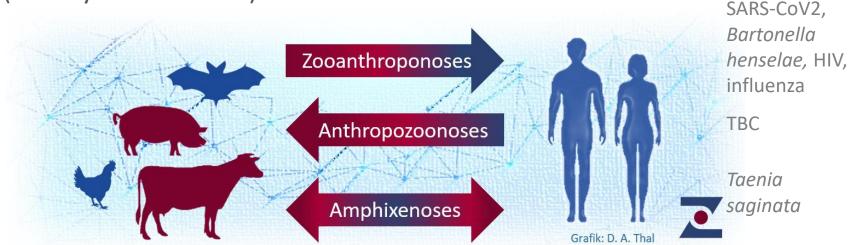


Can you give examples of zoonoses?

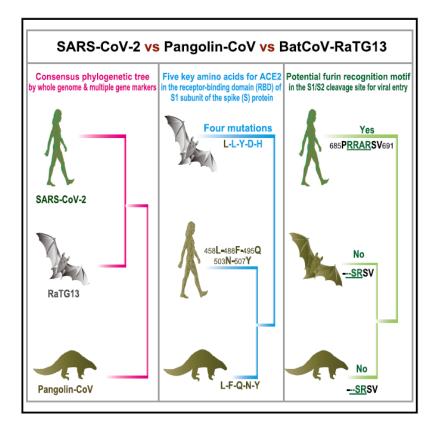


What is a zoonosis?

- Greek 'zoon' (animal) and 'nosos' (disease)
- An **infectious disease**, caused by a **pathogen** (bacterium, virus, helminth, protozoa, fungus or prion) that has **jumped** from an animal (usually a **vertebrate**) to a **human**



Possible Pangolin Origin of SARS-CoV-2



- 1) Pangolin-CoV is 91.02% identical to SARS-CoV-2 at the whole-genome level
- Pangolin-CoV is the second closest relative of SARS-CoV-2 behind RaTG13
- 3) Five key amino acids in the Receptor Binding Domain are consistent between Pangolin-CoV and SARS-CoV-2
- 4) Only SARS-CoV-2 contains a potential cleavage site for furin proteases



4

Zhang et al., 2020, Current Biology 30, 1–6 https://doi.org/10.1016/j.cub.2020.03.022

Wikipedia list zoonoses

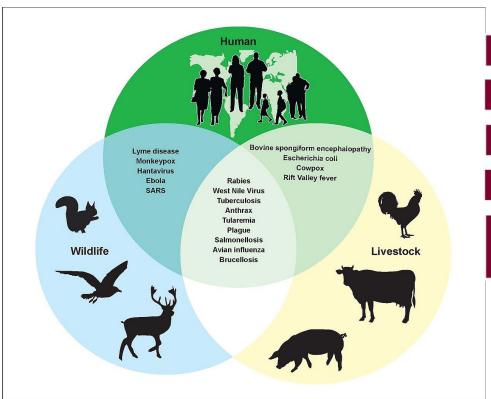
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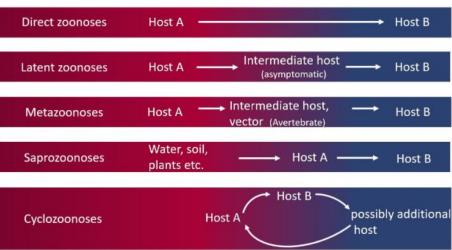
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Disease ^[56]	Pathogen(s)	Animals involved	Mode of transmission	Emergence
African sleeping sickness	Trypanosoma brucei rhodesiense	range of wild animals and domestic livestock	transmitted by the bite of the tsetse fly	'present in Africa for thousands of years' – major outbreak 1900–1920, cases continue (sub-Saharan Africa, 2020)
Angiostrongyliasis	Angiostrongylus cantonensis, Angiostrongylus costaricensis	rats, cotton rats	consuming raw or undercooked snails, slugs, other mollusks, crustaceans, contaminated water, and unwashed vegetables contaminated with larvae	
Anisakiasis	Anisakis	whales, dolphins, seals, sea lions, other marine animals	eating raw or undercooked fish and squid contaminated with eggs	
Anthrax	Bacillus anthracis	commonly – grazing herbivores such as cattle, sheep, goats, camels, horses, and pigs	by ingestion, inhalation or skin contact of spores	
Babesiosis	Babesia spp.	mice, other animals	tick bite	
Baylisascariasis	Baylisascaris procyonis	raccoons	ingestion of eggs in feces	
Barmah Forest fever	Barmah Forest virus	kangaroos, wallabies, opossums	mosquito bite	
Bird flu	Influenza A virus subtype H5N1	wild birds, domesticated birds such as chickens ^[57]	close contact	2003–19 Avian Influenza in Southeast Asia and Egypt
Bovine spongiform encephalopathy	Prions	cattle	eating infected meat	isolated similar cases reported in ancient history; in recent UK history probable start in the 1970s ^[58]
Brucellosis	Brucella spp.	cattle, goats, pigs, sheep	infected milk or meat	historically widespread in Mediterranean region; identified early 20th century
Bubonic plague, Pneumonic plague, Septicemic plague, Sylvatic plague	Yersinia pestis	rabbits, hares, rodents, ferrets, goats, sheep, camels	flea bite	Epidemics like Black Death in Europe around 1347–53 during the Late Middle Age, Third Plague Pandemic in China-Qing dynasty and India alone
Capillariasis	Capillaria spp.	rodents, birds, foxes	eating raw or undercooked fish, ingesting embryonated eggs in fecal-contaminated food, water, or soil	
Cat-scratch disease	Bartonella henselae	cats	bites or scratches from infected cats	



Possibilities for zoonotic disease transmission







Source: GAO analysis of USGS data (data); Art Explosion (images).





Your patient consults for painful hallux valgus but mentions he is bitten by a bat 3 months ago. What do you do?





Press S to show image



Table 1. Investigated bats	, the Netherlands,	1984–2003
	No enocimone	Lyccoviru

	No oposimono	Lypopyirus antigan
Bat species	No. specimens tested	Lyssavirus antigen positive (%)
Eptesicus serotinus	1,219	251 (20.6)
E. nilssonii	1	0
Myotis mystacinus	18	0
M. nattereri	9	0
M. daubentonii	111	0
M. dasycneme	129	5 (3.9)
Pipistrellus pipistrellus	1,837	0
P. nathusii	256	0
Nyctalus noctula	61	0
N. leisleri	3	0
Plecotus auritus	214	0
Vespertilio murinus	6	0
Undetermined	9	0
Total	3,873	256





Rabies

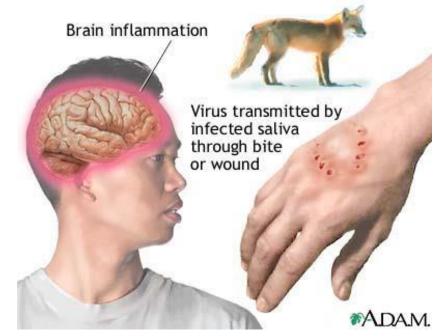
"Golden window"

Incubation average 20-90 days

Extreme incubation times : 6 days to 6 years

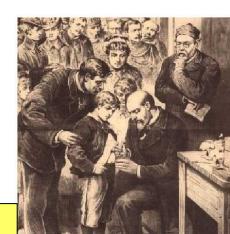
Bites close to face have shorter incubation period

Prodroma during 2-10 days



Rabies: treatment if no symptoms yet

- Initially: **Clean** wound with soap or detergent
 - Anti-tetanus prophylaxis
 - Antibiotics optional
- Antirabies hyperimmune globulines
 - As much as local possible around wound
 - Best humane 20 IE/kg (expensive; respect dose)
 - √ Has to be given < 8 days after vaccination</p>
- Vaccination: Louis Pasteur 1885
 - → Possible because of long incubation period



WHO EXPOSURE RISK CATEGORIES

Category I

Category II

Superficial lesions from scratches or grazes, without bleeding. Licking of non-intact skin

Licking a grazed or broken skin

Category III Single or multiple bites or scratches that penetrate the dermis Contact with the mucous membranes via the saliva after licking

Licking of the intact skin In other words: no exposure

Tactile contact (stroking) or feeding the animal

Gnawing the uncovered and originally intact skin

Vaccine schedule

- Schedule 1: D0, D3
 - Schedule 2: D0 (2x),D7, D21
 - Schedule 3: D0, D3, D7,
 - D14, D28 + RIG D0

INSTITUTE OF TROPICAL MEDICIN

Non-endemic: Suspected

Non-endemic:

Not suspected

Endemic

Non-endemic:

Suspected

Non-endemic:

Not suspected

Endemic and

non-endemic:

(Imported fewer than 12 months previously) Non-endemic: CATEGORY I

None

None

None

None

None

None

None

None

None* or

Schedule 3

CATEGORY II

SCHEDULE 2

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None

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None

SCHEDULE 3

CATEGORY III

SCHEDULE 3

SCHEDULE 3

None

SCHEDULE 2

SCHEDULE 3

SCHEDULE 3

SCHEDULE 3

None

SCHEDULE 3

WILD LAND MAMMALS SUCH AS FOX, WOLF, RACOON ...

MONKEY (WILD)

DOG, CAT, FERRET

BAT

IMMUNE SUPPRESSION

CATEGORIES II and III

SCHEDULE 3

SCHEDULE 3

None

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SCHEDULE 3

Rabies-PrEP in

good order

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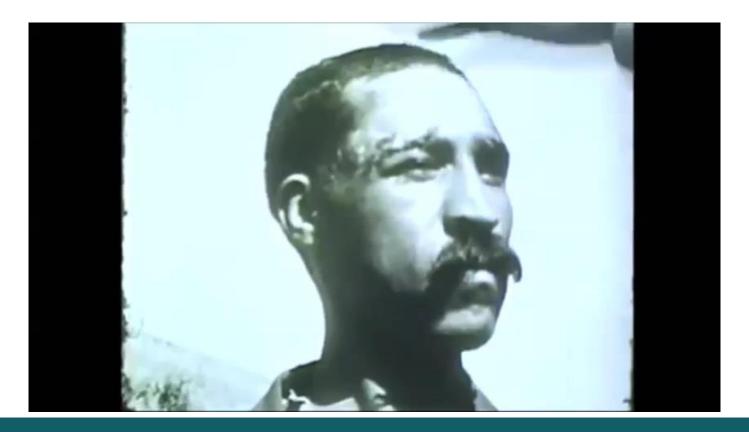
None

SCHEDULE

ANIMALS

D7, Endemic

The patient develops hydrophobia. What do you do?





Jeanna Giese: Milwaukee protocol

2005: 1° ever Rabies survivor





Milwaukee protocol

- Ketamine (anti-NMDA)
- Midazolam
- Ribavirin
- Amantadin (anti-Parkinson drug → dopamine ↑; in-vitro anti rabies action)
- + vaccine +/- IgG's

- → Revised protocol: without ribavirin
- Survivors: 2/25 first protocol, 2/10 new protocol

Coma

Woman, 48 years

- Muscle pain and an elevated body temperature 2 weeks after a tick bite on her right hip
- COVID-19 testing –
- GP: antibiotics
- A few days later, hospitalization with asthenia, tremor, drowsiness, and fever
 - peripheral facial palsy
 - brachial weakness
 - nuchal rigidity
- CSF: WBC 37/μl, prot +
- Borrelia serology and PCR –
- MRI: demyelinating lesions and encephalopathy
- EEG: diffuse slow activity



Which diagnostic test would you ask to confirm your suspicion?



Arboviruses

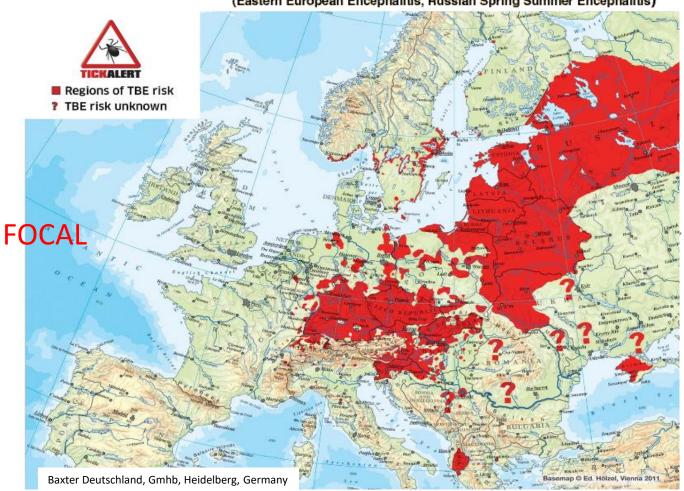
- Togaviridae
 - Alphavirus : EEE, WEE, VEE, Ross River, Chikungunya
- Flaviviridae
 - Yellow Fever, Dengue, Japanese Encephalitis, West Nile
 - TBEV, msk HF, Kyasanur FD (sim. Alkhurma virus)
- Bunyaviridae
 - Bunyaviruses : California Encephalitis, Hantavirus
 - Nairoviruses : CCHF
 - Phleboviruses : Rift Valley, Phlebotomus Fever



Epidemiology

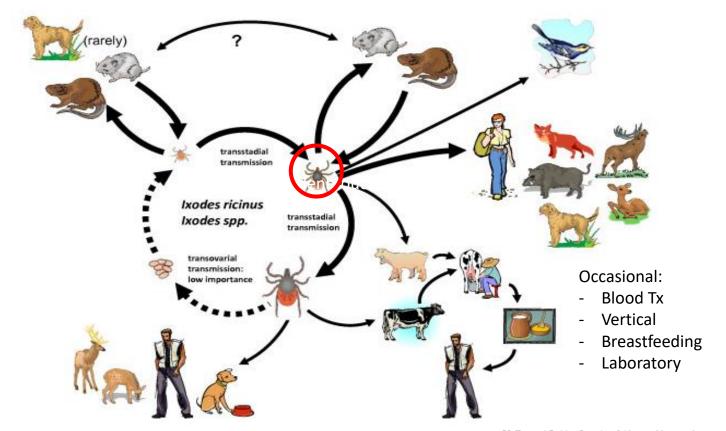
TBE - Tick Borne Encephalitis

(Eastern European Encephalitis, Russian Spring Summer Encephalitis)



Transmission

WITHIN MINUTES → early removal does NOT prevent disease!!!



Pfeffer and Dobler Parasites & Vectors 2011, 4:59 http://www.parasitesandvectors.com/content/4/1/59

Overview of tick genera in the three families

1. Argasidae : Argas, Ornithodoros, Otobius, Antricola, Nothoaspis

2. Ixodidae : Amblyomma, Aponomma, Boophilus, Cosmiomma,

Dermacentor, Haemaphysalis, Hyalomma Ixodes, Margaropus,

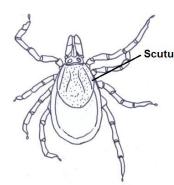
Nosomma, Rhipicentor, Rhipicephalus

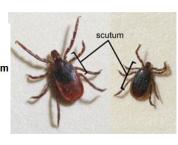
3. Nutal iellidae : only 1 species, rare

Soft ticks: no scutum = dorsal shield



Hard ticks: scutum





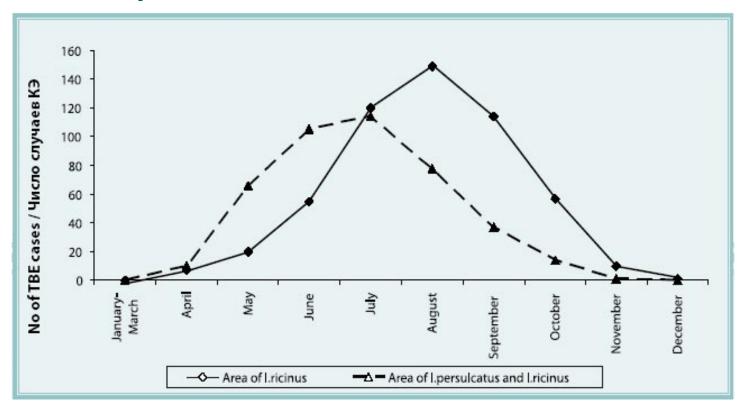
Other pathogens transmitted by ticks

- Lyme (Borrelia Burgdorferi/Afzelii, Garinii)
- Anaplasma
- Ehrlichia
- Bartonella
- Babesia
- Rickettsia: RMSF, R. conori, Japanese spotted fever,...
- Tularemia: Francisella tularensis
- Colorado Tick fever
- Hemorragic fevers: Crimean-Congo, Omsk,...
- TBRL: Tick Born Relapsing Fever (B. duttonii, hermsii,...) = soft tick





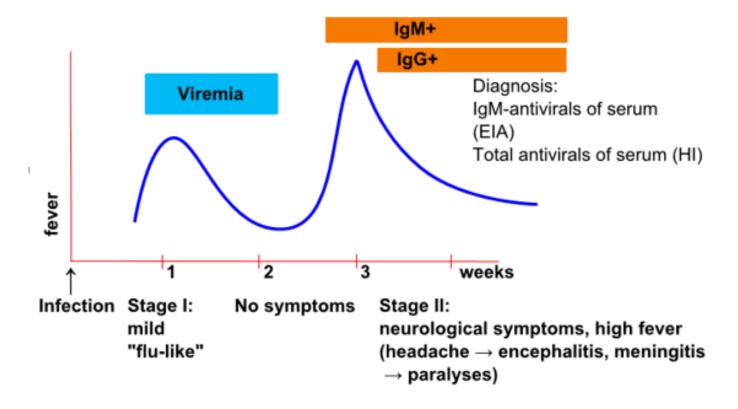
TBE, seasonality



Veera Vasilenko, Kuulo Kutsar, Irina Golovljova, http://www.epinorth.org/, Nat Inst for Health Development, Tallinn, Estonia



Diagnosis





Diagnostic pitfalls

- Vaccination status? And JE, YF vaccination?
- IgM present after 1° and 2° vaccination
- Cross reaction with other flaviviruses

- IgM > 500 AU
- VNT

- CSF not always IgM/G present
- CSF: early-on neutrophiles may predominate
- IgM detectable up to ≥ 10 months, IgG persist for life



Autochthonous Cases of Tick-Borne Encephalitis, Belgium, 2020

Anke Stoefs, Leo Heyndrickx, Jonathan De Winter, Evelien Coeckelbergh, Barbara Willekens, Alicia Alonso-Jiménez, Anne-Marie Tuttino, Yvette Geerts, Kevin K. Ariën, Marjan Van Esbroeck

Table. Laboratory results confirming TBEV infections in 3 autochthonous human cases, Belgium, 2020								
Case	Symptom	Expos	Sample type, days	Flavivirus IFA		PRNT ₉₀		
no.	onset date	Likely site, postal code Likely route, time		after symptom onset	IgM†	lgG‡	titer	rRT-PCR
1	Jun 5	Oostkamp, 8020	Tick bite, 2 wk before	Serum, 5	TBEV+	TBEV+	1:25	ND
		symptom onset		CSF, 6	TBEV+	TBEV+	ND	ND
2	Jun 21	Lille, 2275 Tick bite, 2 wk before		CSF, 18	TBEV+	TBEV+	ND	ND
			symptom onset		TBEV+	TBEV+	1:60	ND
3	Jul 20	Wanze, 4520 Multiple tick bites in		Serum, 2	_	_	ND	+
		the weeks before		Serum, 18	TBEV+	TBEV+	1:194	ND

^{*}CSF, cerebrospinal fluid; IFA, immunofluorescence assay; ND, not done; PRNT₉₀, plaque reduction neutralization testing at 90% sensitivity; rRT-PCR, real-time reverse transcription PCR; TBEV, tick-borne encephalitis virus; +, positive; –, negative.



[†]Only TBEV-positive on the flavivirus mosaic IFA.

[‡]Also positive signal for ≥1 other flavivirus on the mosaic IFA, including West Nile virus, Japanese encephalitis virus, yellow fever virus, and dengue virus serotypes 1–4.



Figure. Geographic distribution of autochthonous human cases of tick-borne encephalitis, Belgium and the Netherlands (adapted from National Institute of Public Health and Environment [10]). Grey shading indicates communities in Belgium in which antibodies against tick-borne encephalitis virus have been detected in animals (adapted from S. Roelandt [2]).

Case continuation

Several months later still weakness of her right arm, loss of cognitive function, inability to concentrate, fatigue, and tremor



Prevention

Protect Yourself Against Lyme Disease in Spring, Summer, and Fall







Vaccination

Table 3-19. Tickborne encephalitis (TBE) vaccines licensed in Europe and Russia ¹						
TRADE NAME (MANUFACTURE R, LOCATION)	AGE (Y)	DOSE	ROUTE	PRIMARY SERIES	FIRST BOOSTER (Y)	SUBSEQUENT BOOSTERS (Y)
FSME-IMMUN (Baxter, Austria)	≥16	0.5 mL	IM	3 doses (0, 1–3 mo, 6–15 mo) ²	d .	53
FSME-IMMUN Junior (Baxter, Austria)	1-15	0.25 mL	IM	3 doses (0, 1–3 mo, 6–15 mo) ²	3	5
Encepur-Adults (Novartis, Germany)	≥17	0.5 mL	IM	3 doses (0, 1–3 mo, 9–12 mo) ⁴	3	5 ³
Encepur-Children (Novartis, Germany)	1-11	0.25 mL	IM	3 doses (0, 1–3 mo, 9–12 mo) ⁴	3	5
EnceVir (Microgen, Russia)	≥3	0.5 mL	IM	2 doses (0, 5–7 mo) ⁵	1	3
TBE-Moscow (Chumakov Institute, Russia)	≥3	0.5 mL	IM	2 doses (0, 1–7 mo)	1	3

- Interchangeable
- Accelerated schemes
- No herd immunity
- Cave: Breakthrough











You patient tell you that he's dog is diagnosed with Leptospirosis.





Press S to show image



You patient tell you that he's dog is diagnosed with Leptospirosis. He plays a lot with your small children and has the habit of licking their mouth when they eat candies. What do you do?





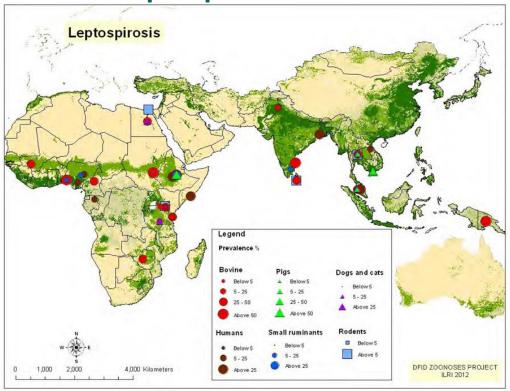
Symptoms of Leptospirosis in Dogs

- Lethargy and depression
- Vomiting
- Diarrhea
- Dehydration
- Fever
- A runny nose
- Red eyes
- A cough
- Muscle pain
- Shivering
- Jaundice
- Kidney or liver failure

East Shore's Veterinary Services



Leptospirosis = zoonosis

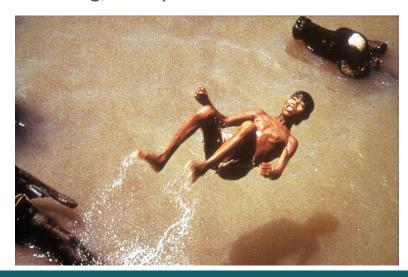


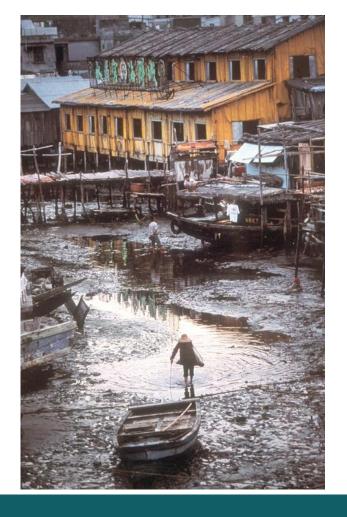
More data on animals than on humans available...



Leptospirosis: Transmission

- Via contaminated urine & <u>fresh</u> water
 - Rats, voles, moles,...
 - Dogs, cattle, raccoons, ...
- Flooding, heavy rains







Leptospirosis is ubiquitous...

SURVEILLANCE AND OUTBREAK REPORT

An outbreak of leptospirosis among kayakers in Brittany, North-West France, 2016

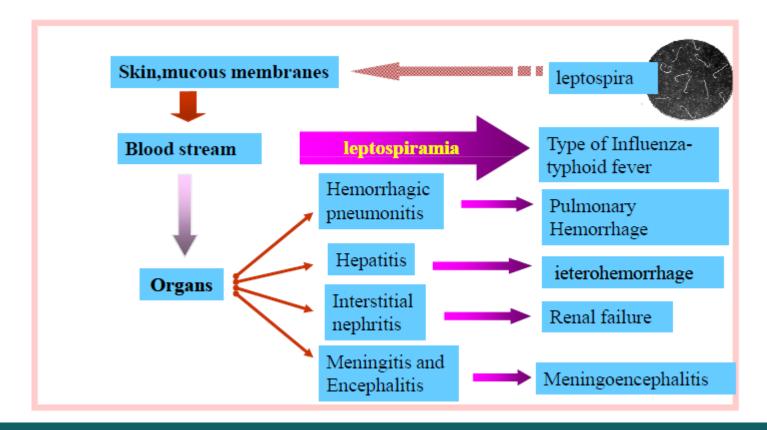
Yvonnick Guillois¹, Pascale Bourhy², Florence Ayral³, Mathilde Pivette¹, Anouk Decors⁴, José Héctor Aranda Grau⁵, Benoît Champenois⁵, Célia Malhère⁶, Benoît Combes⁷, Céline Richomme⁸, Marine Le Guyader³, Lisa Antoinette King¹, Alexandra Septfons^{9,10}



Vrees voor massale besmetting rattenziekte na Titan Run



Pathogenesis

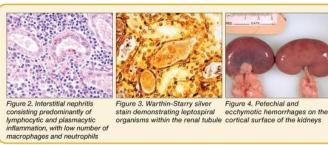


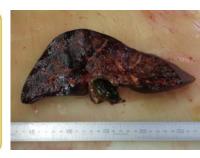


Leptospirosis: symptoms









Conjunctival suffusion (= redness without inflammatory excudates)

+/- conjunctival hemorrhage +/- icterus

ARDS +/pulmonary hemorrhage

Interstitital nephritis

- Proteinuria
- Pyuria
- Hematuria
- Granular casts

Acute renal failure, usually nonoliguric

Hepatitis with transaminases ++ Jaundice Sometimes acute fulminant liver with coagulation deficits

Barnacle et al. Journal of Intensive Care

Today's Veterinary Practice July/August 2012



Leptospirosis: treatment

Mostly self-limiting

Reality: severely ill patient, MOF

→ empiric antibiotics for 'sepsis', 'meningitis'

- Mild disease: AB benefit controversial
 - Doxycycline 100 mg 2x1, 7d
 - Alt: azithromycin 500 mg 1x1, 3d or amoxicillin 500 mg 3x1, 7d
- Severe disease:
 - Penicillin G 1,5 M U IV 4x/d, 7d
 - Ceftriaxone 1-2 g IV 1x/d, 7d
 - Doxycycline 100 mg IV 2x/d, 7d

Role of IV corticosteroids not proven



Human contacts?

5.3 Prophylaxis and treatment of human contacts

There is no commercially available value for humans.

Pre-exposure prophylaxis may be beneficial for people who will be experiencing exposures that carry a high risk of infection. These include soldiers training in tropical regions, adventure tourists who will have freshwater exposure (especially tropical) and veterinarians who will be working with infected animals. Doxycycline at 200mg once for a single exposure or once a week throughout ongoing exposure is recommended (Brown 2008, Guidugli 2000, Heymann 2004).

Antibiotic post-exposure prophylaxis (e.g. doxycycline at 200 mg) is indicated for persons who have been exposed to leptospires. However, antibiotic prophylaxis is not routilely offered to protect owners of animals which have been infected with leptosphosis as the risk of transmission through normal human contact with animals is considered low (e.g. if there is no physical contact with the animal's urine) (Brown 2008, Heymann 2004).

Doxycycline prophylaxis is contra-indicated in pregnant or breast-feeding women and children under the age of 8. As indicated, it may be prudent for these individuals to avoid clean-up of animal wastes and contact with pets during peak periods of transmission (1-3 weeks after onset).

Prompt antibiotic treatment of human cases can reduce the duration of fever, but may not reduce mortality. Penicillin is the drug of choice, but alternatives are doxycycline, ampicillin, erythromycin, cephalosporins and quinalone antibiotics (Heymann 2004).



Questions?



