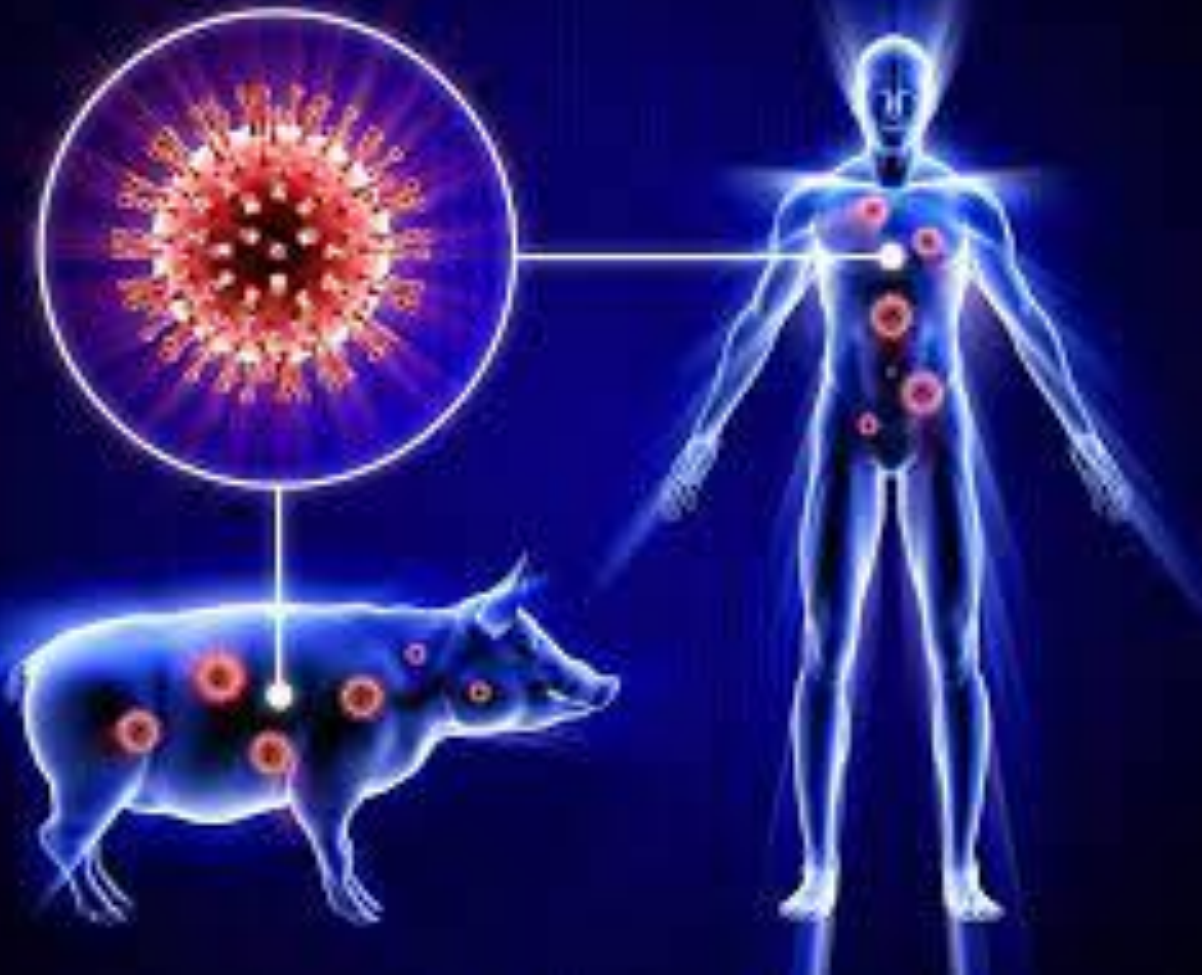


ZOÖNOSES



STEVEN VAN DEN BROUCKE

NAJAARSYMPOSIUM
KARVA 27-11-2021



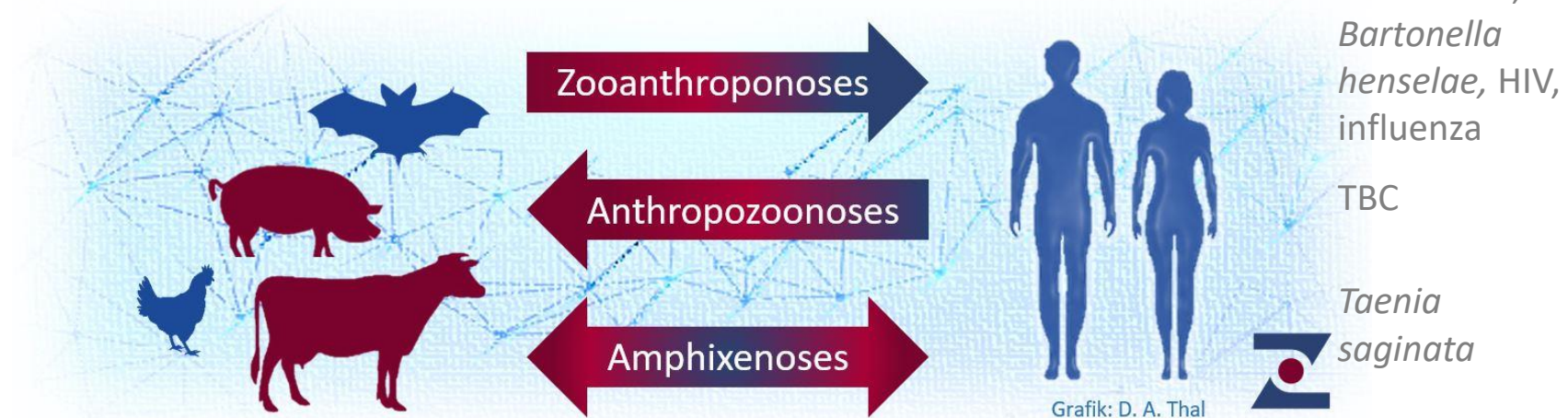
Can you give examples of zoonoses?

Press S to show image

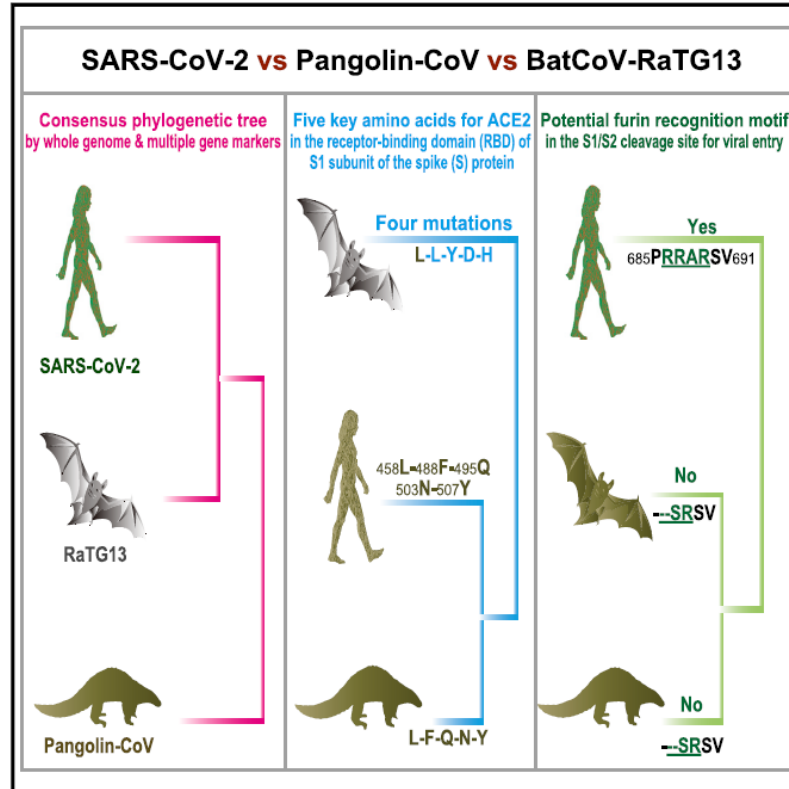


What is a zoonosis?

- 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
- 2) 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



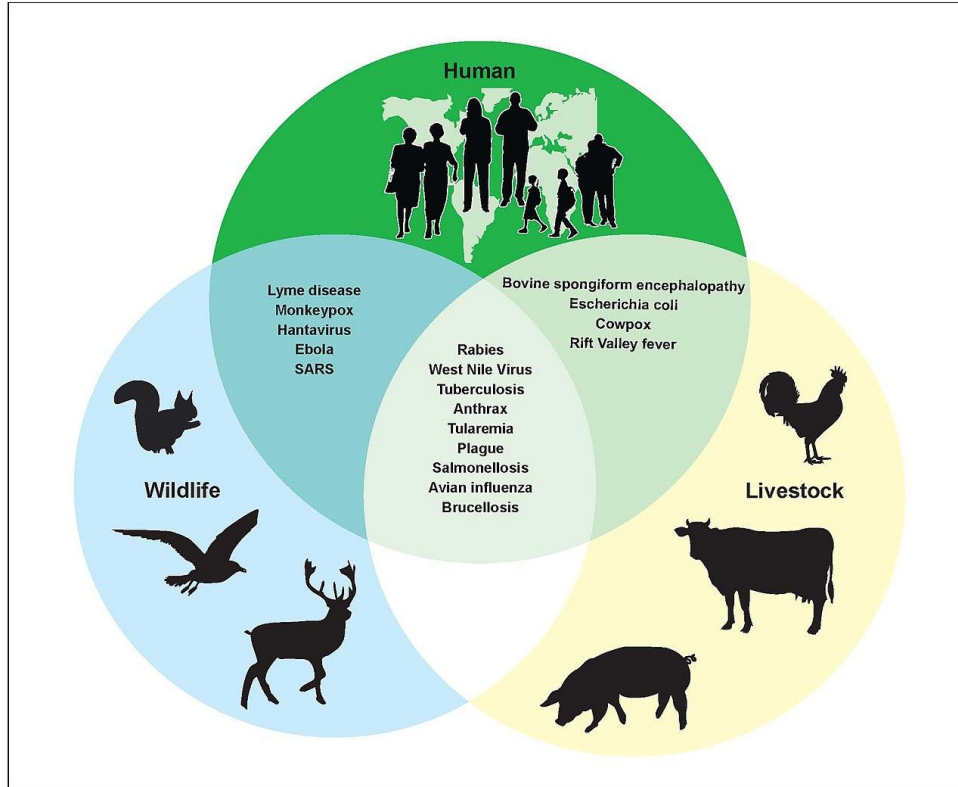
■ 70 pathogens

[illegible]

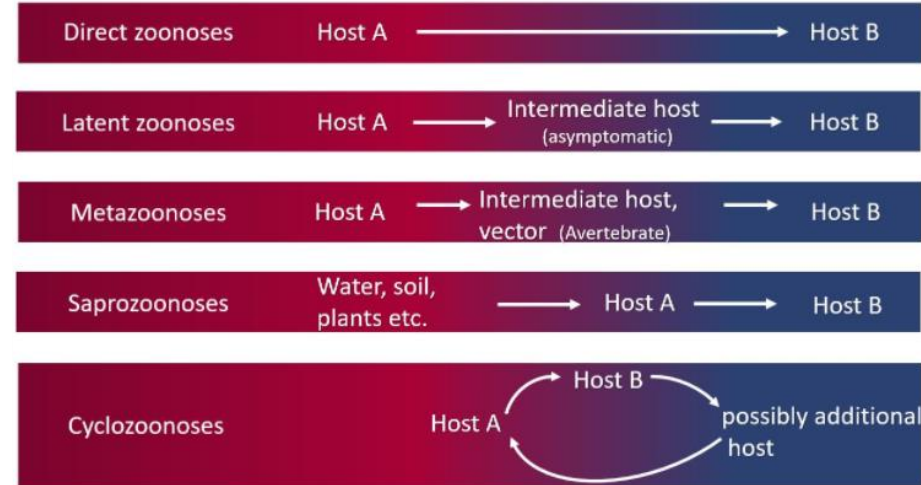
Disease ^[66]	Pathogen(s)	Animals involved	Mode of transmission	Emergence
African sleeping sickness	<i>Trypanosoma brucei rhodesiense</i>	range of wild animals and domestic livestock	transmitted by the bite of the tsetse fly	'present in Africa for thousands of years' – major outbreak 1900–1920, cases continue (sub-Saharan Africa, 2020)
Angiostrongyliasis	<i>Angiostrongylus cantonensis</i> , <i>Angiostrongylus costaricensis</i>	rats, cotton rats	consuming raw or undercooked snails, slugs, other mollusks, crustaceans, contaminated water, and unwashed vegetables contaminated with larvae	
Anisakiasis	<i>Anisakis</i>	whales, dolphins, seals, sea lions, other marine animals	eating raw or undercooked fish and squid contaminated with eggs	
Anthrax	<i>Bacillus anthracis</i>	commonly – grazing herbivores such as cattle, sheep, goats, camels, horses, and pigs	by ingestion, inhalation or skin contact of spores	
Babesiosis	<i>Babesia</i> spp.	mice, other animals	tick bite	
Baylisascariasis	<i>Baylisascaris procyonis</i>	raccoons	ingestion of eggs in feces	
Barmah Forest fever	<i>Barmah Forest virus</i>	kangaroos, wallabies, opossums	mosquito bite	
Bird flu	Influenza A virus subtype H5N1	wild birds, domesticated birds such as chickens ^[67]	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	<i>Brucella</i> 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	<i>Yersinia pestis</i>	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	<i>Capillaria</i> spp.	rodents, birds, foxes	eating raw or undercooked fish, ingesting embryonated eggs in fecal-contaminated food, water, or soil	
Cat-scratch disease	<i>Bartonella henselae</i>	cats	bites or scratches from infected cats	



Possibilities for zoonotic disease transmission



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



Go to www.menti.com and use the code 5943 5798

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



0	0	0	0
Prescribe NSAIDS and refer to a podologist	Option A + series of 5 anti-rabies vaccines	Option B + anti- rabies immunoglobulines IM?	Something else

Press S to show image



Table 1. Investigated bats, the Netherlands, 1984–2003

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



Rabies

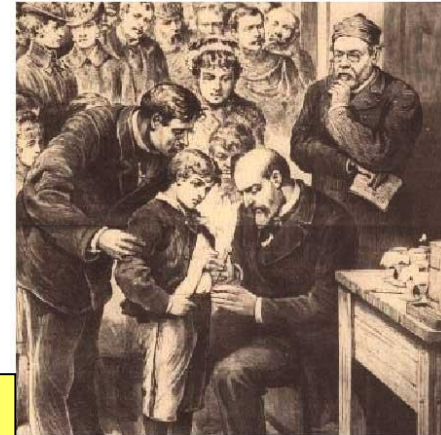
“Golden window”

- 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
- **Vaccination** : Louis Pasteur 1885
 - Possible because of long incubation period



Emile Roux vaccinating Joseph Meister. Pasteur looks on

WHO EXPOSURE RISK CATEGORIES

Category I

- Tactile contact (stroking) or feeding the animal
- Licking of the intact skin

In other words: no exposure

Category II

- Gnawing the uncovered and originally intact skin
- Superficial lesions from scratches or grazes, without bleeding.
- Licking of non-intact skin

Category III

- Single or multiple bites or scratches that penetrate the dermis
- Contact with the mucous membranes via the saliva after licking
- Licking a grazed or broken skin
- (Possible) scratches and bites of bats: often no visible lesion or the feeling of a bite



Vaccine schedule

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

ANIMALS	CATEGORY I	CATEGORY II	CATEGORY III	IMMUNE SUPPRESSION CATEGORIES II and III	Rabies- PrEP in good order
WILD LAND MAMMALS SUCH AS FOX, WOLF, RACCOON ...					
Endemic	None	SCHEDULE 2	SCHEDULE 3	SCHEDULE 3	SCHEDULE 1
Non-endemic: Suspected	None	SCHEDULE 2	SCHEDULE 3	SCHEDULE 3	SCHEDULE 1
Non-endemic: Not suspected	None	None	None	None	None
MONKEY (WILD)					
Endemic	None	SCHEDULE 2	SCHEDULE 2	SCHEDULE 3	SCHEDULE 1
DOG, CAT, FERRET					
Endemic	None	SCHEDULE 2	SCHEDULE 3	SCHEDULE 3	SCHEDULE 1
Non-endemic: (Imported fewer than 12 months previously)	None	SCHEDULE 2	SCHEDULE 3	SCHEDULE 3	SCHEDULE 1
Non-endemic: Suspected	None	SCHEDULE 2	SCHEDULE 3	SCHEDULE 3	SCHEDULE 1
Non-endemic: Not suspected	None	None	None	None	None
BAT					
Endemic and non-endemic:	None* or Schedule 3	SCHEDULE 3	SCHEDULE 3	SCHEDULE 3	SCHEDULE 1



The patient develops hydrophobia. What do you do?

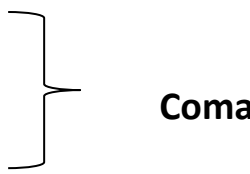


Jeanna Giese: Milwaukee protocol

■ 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
- 
- Coma

→ Revised protocol: without ribavirin

- Survivors: 2/25 first protocol, 2/10 new protocol

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/ μ l, prot +
- *Borrelia* serology and PCR –
- MRI: demyelinating lesions and encephalopathy
- EEG: diffuse slow activity



Go to www.menti.com and use the code 5943 5798

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, Omsk HF, Kyasanur FD (sim. Alkhurma virus)

■ Bunyaviridae

- Bunyaviruses : California Encephalitis, Hantavirus
- Nairoviruses : CCHF
- Phleboviruses : Rift Valley, Phlebotomus Fever



Epidemiology

TBE - Tick Borne Encephalitis

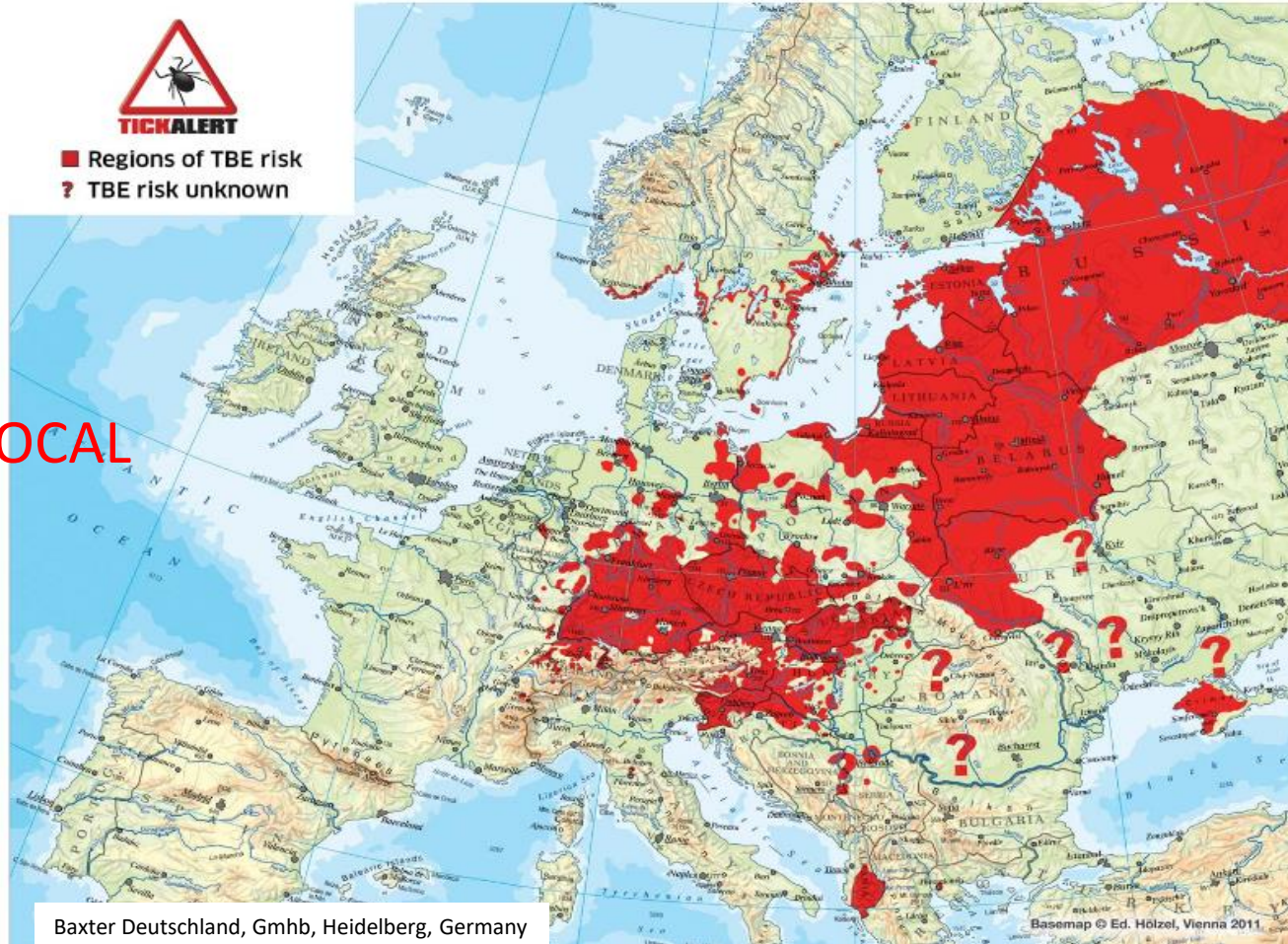
(Eastern European Encephalitis, Russian Spring Summer Encephalitis)



■ Regions of TBE risk

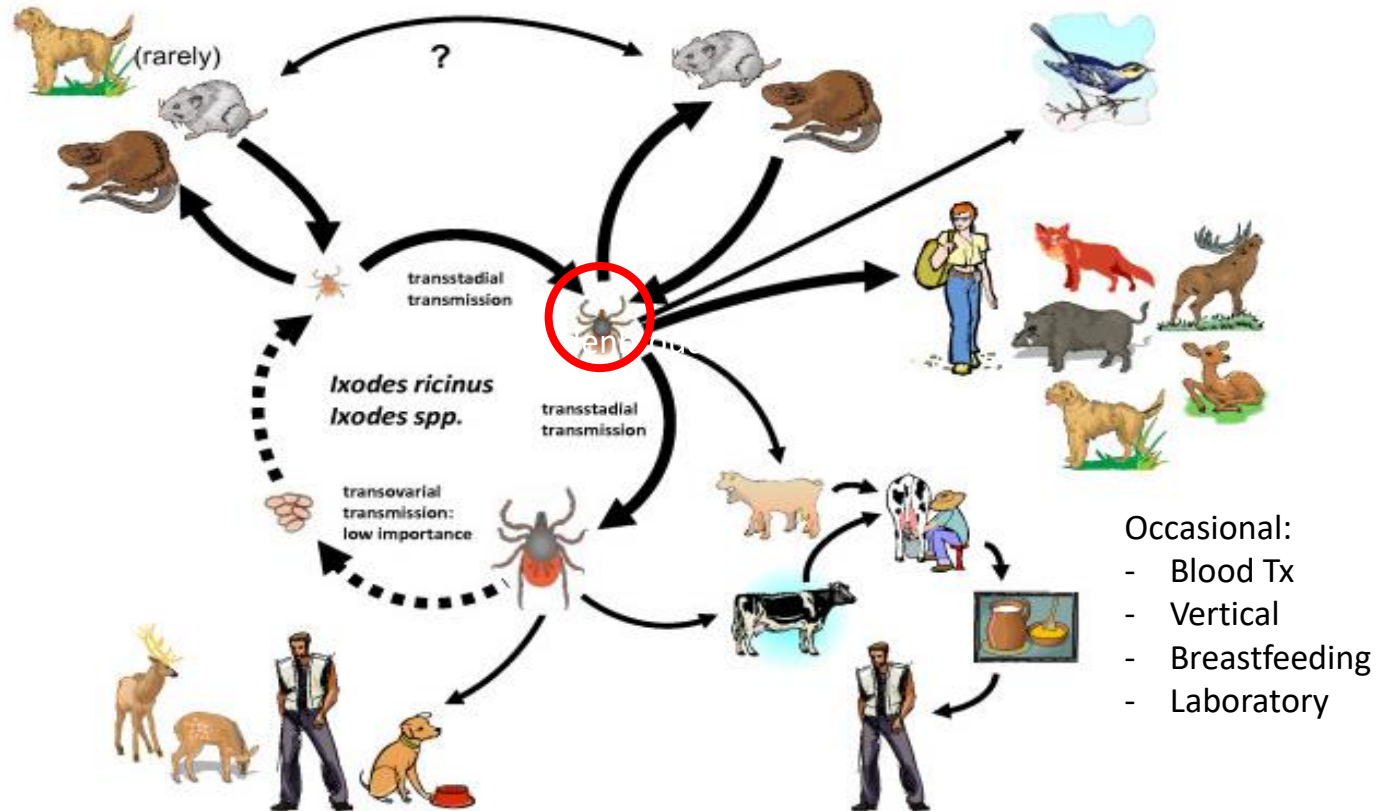
■ TBE risk unknown

FOCAL



Transmission

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



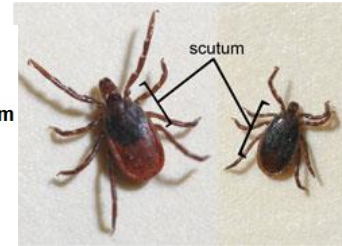
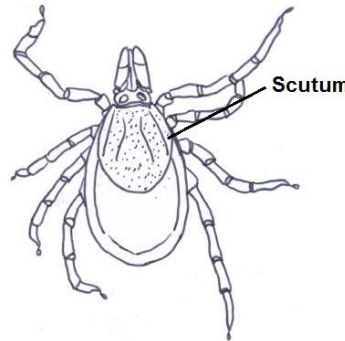
Overview of tick genera in the three families

1. Argasidae : *Argas*, *Ornithodoros*, *Otobius*, *Antricola*, *Nothoaspis*
2. Ixodidae : *Amblyomma*, *Aponomma*, *Boophilus*, *Cosmiomma*, *Dermacentor*, *Haemaphysalis*, *Hyalomma*, *Ixodes*, *Margaropus*, *Nosomma*, *Rhipicentor*, *Rhipicephalus*
3. Nuttalliellidae : only 1 species, rare

Soft ticks: no scutum = dorsal shield



Hard ticks: scutum



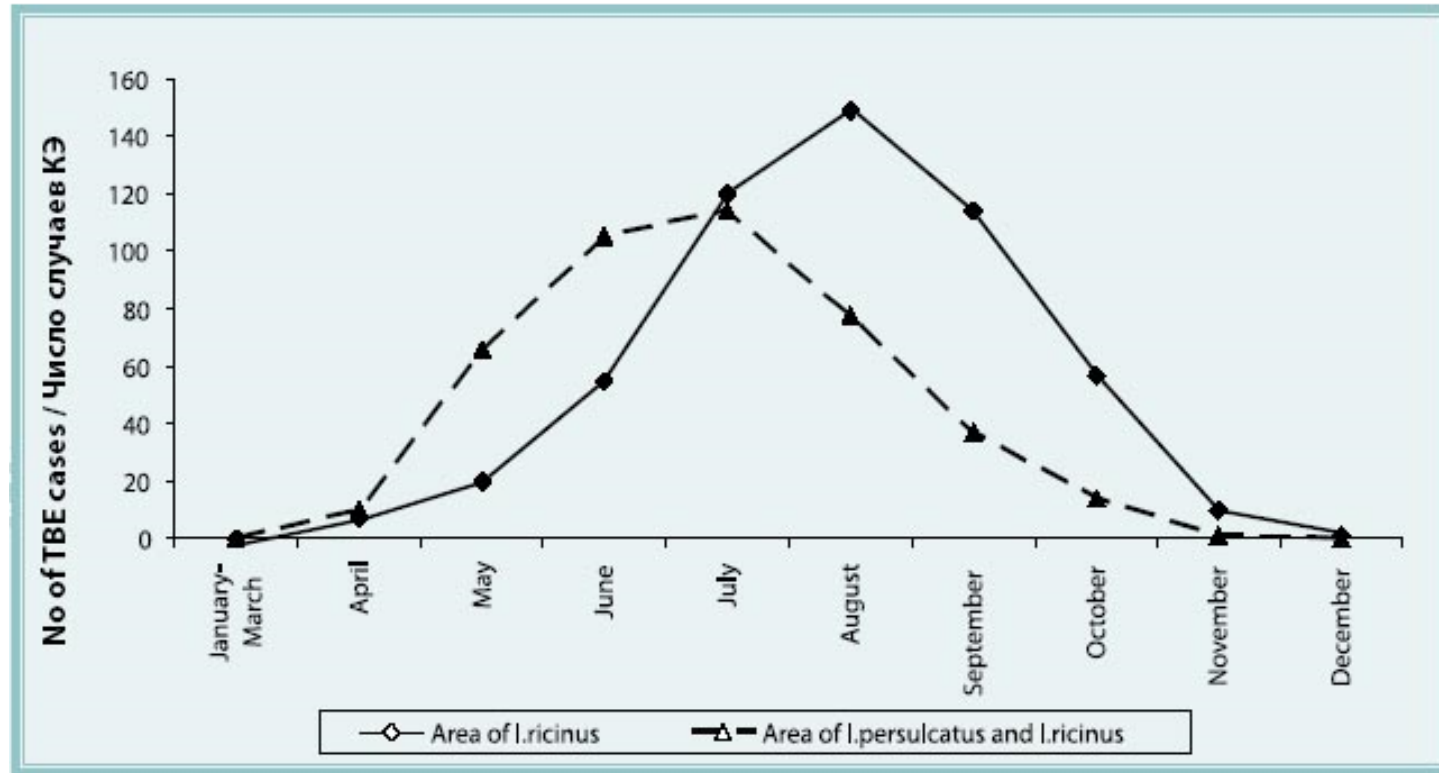
Other pathogens transmitted by ticks

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



A tularemia lesion on the dorsal skin of the right hand

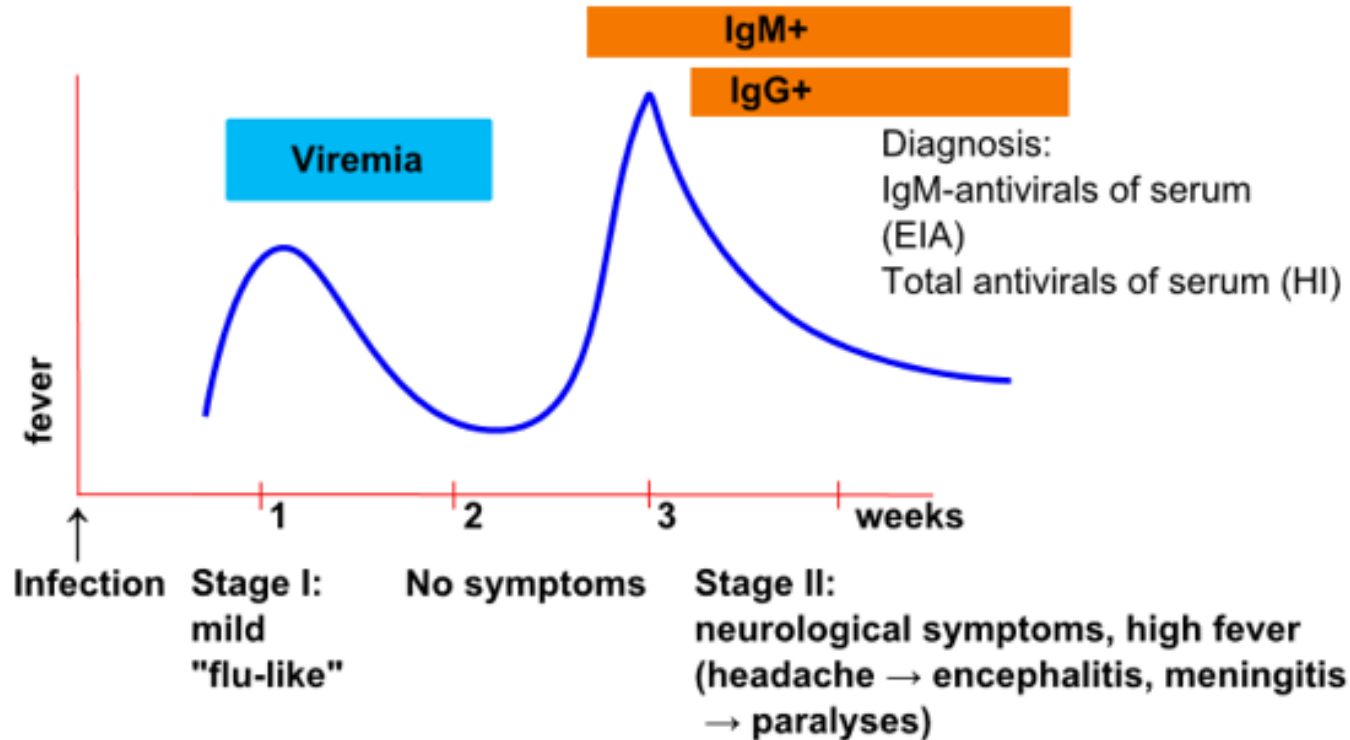
TBE, seasonality



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 neutrophils 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 no.	Symptom onset date	Exposure		Sample type, days after symptom onset	Flavivirus IFA		PRNT ₉₀ titer	rRT-PCR
		Likely site, postal code	Likely route, time		IgM†	IgG‡		
1	Jun 5	Oostkamp, 8020	Tick bite, 2 wk before symptom onset	Serum, 5	TBEV+	TBEV+	1:25	ND
				CSF, 6	TBEV+	TBEV+	ND	ND
2	Jun 21	Lille, 2275	Tick bite, 2 wk before symptom onset	CSF, 18	TBEV+	TBEV+	ND	ND
				Serum, 20	TBEV+	TBEV+	1:60	ND
3	Jul 20	Wanze, 4520	Multiple tick bites in the weeks before symptom onset	Serum, 2	–	–	ND	+
				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.





Case continuation

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

1 Walk in the middle of trails, away from tall grass and bushes.

2 Wear a long-sleeved shirt.

3 Wear white or light-colored clothing to make it easier to see ticks.

4 Wear a hat.

5 Spray tick repellent on clothes and shoes before entering woods.

6 Wear long pants tucked into high socks.

7 Wear shoes—no bare feet or sandals.



Vaccination

Table 3-19. Tickborne encephalitis (TBE) vaccines licensed in Europe and Russia¹

TRADE NAME (MANUFACTURER, 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	3	5 ³
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



Go to www.menti.com and use the code 5943 5798

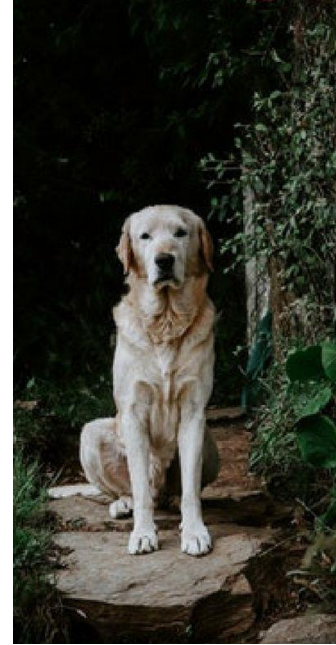
You patient tell you that he's dog is diagnosed with Leptospirosis.

0	0	0	0
Doxycycline for all family members	Nothing	I don't know	Something else

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?

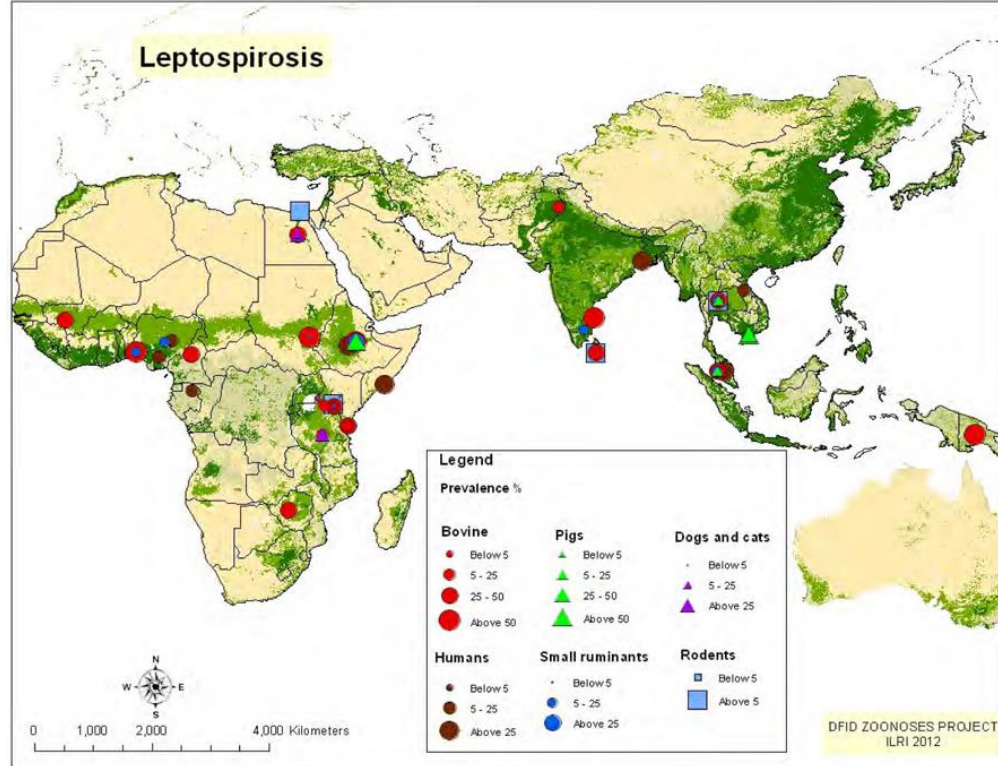


Symptoms of Leptospirosis in Dogs

- 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 & fresh 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 Ayrat³, Mathilde Pivette¹, Anouk Decors⁴, José Héctor Aranda Grau⁵, Benoît Champenois⁵, Célia Malhère⁶, Benoît Combes⁷, Céline Richomme⁸, Marine Le Guyader³, Lisa Antoinette King¹, Alexandra Septfonds^{9,10}



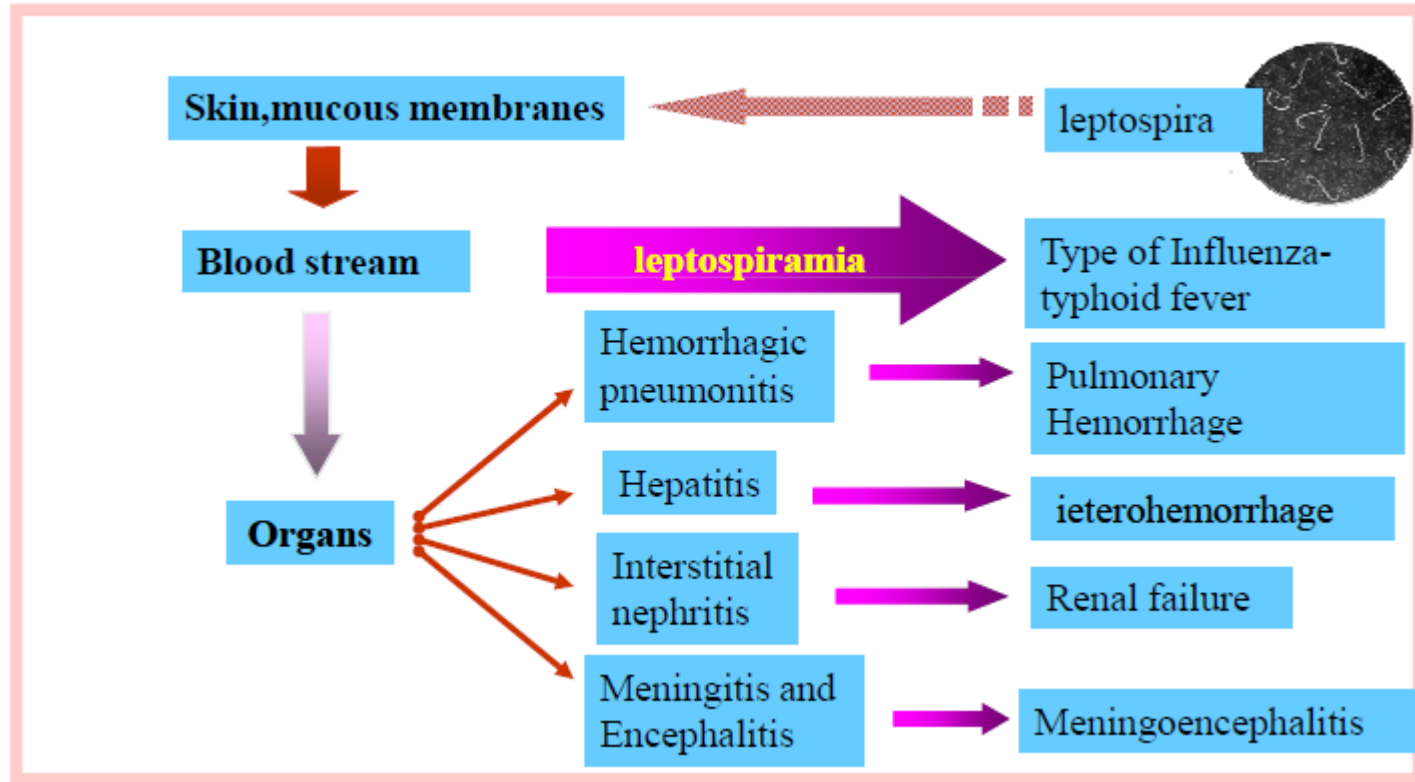
Vrees voor massale besmetting rattenziekte na Titan Run

03/10/2015 om 08:15 door werner rommers

Print



Pathogenesis



Leptospirosis : symptoms

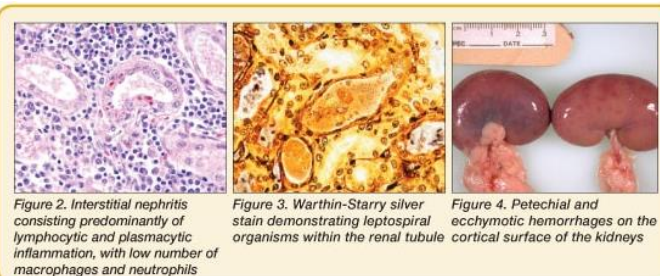


Conjunctival suffusion (= redness without inflammatory exudates)

+/- conjunctival hemorrhage
+/- icterus



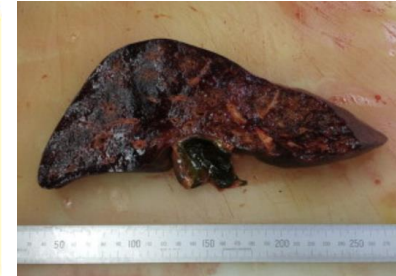
ARDS +/-
pulmonary hemorrhage



Interstitial nephritis

- Proteinuria
- Pyuria
- Hematuria
- Granular casts

Acute renal failure, usually nonoliguric



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

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 ~~vaccine~~ 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 routinely offered to protect owners of animals which have been infected with leptospirosis 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?





**INSTITUTE
OF TROPICAL
MEDICINE
ANTWERP**

SVANDENBROUCKE@ITG.BE