

# **Doctor, I've Been Bitten**

## **6<sup>th</sup> April 2017**

### **Abstracts and References**

#### **Overview of Lyme Disease & Related Infections in the UK**

Dr Matthew Dryden, Rare and Imported Pathogens Laboratory, Public Health England

##### **Learning points**

- Lyme epidemiology in the UK
- Diagnosis
- Presentation
- Treatment of Lyme disease
- Chronic Lyme, does it exist?

Lyme disease has become a controversial and even a fashionable infection. This presentation will review the current epidemiology of borreliosis in the UK, the serological diagnosis, clinical presentation and treatment. It will also touch on the topic of chronic Lyme disease and discuss the phenomenon of this novel plague.

##### **Reference**

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#### **Interactive discussion on difficult cases. The challenge of Lyme disease**

Dr Sandra Pearson

##### **Learning points**

After this lecture participants will be able to:

- Recognise the importance of assessing the pre-test probability of Lyme disease and apply this to clinical practice.
- List the four main pathophysiological processes which have been linked to persistent symptoms after treatment of Lyme disease.
- Recognise the limitations of Lyme serology testing in both confirming and ruling out a diagnosis of Lyme disease.
- Demonstrate awareness of the key known uncertainties in diagnosis and treatment of Lyme disease at systematic review level.
- Demonstrate awareness of the strengths and weaknesses in the evidence base for antibiotic retreatment of persistent symptoms after Lyme disease.
- Recognise the need for further research and outcome studies on the diagnosis and treatment of Lyme disease in a clinical setting.

The diagnosis and treatment of suspected Lyme disease may be challenging especially if patients present months or years after initial infection. The erythema migrans rash may not appear and when

present may be variable in appearance. It may be missed, misdiagnosed or treated with inappropriate or sub-curative antibiotics. The challenges encountered by the Lyme Disease Action (LDA) patient helpdesk have been similar to those found by clinical research conducted in other community-based settings.<sup>1</sup> Clinical diagnosis of suspected cases may be supported by indirect testing using Lyme serology which has inherent limitations in confirming and ruling out Lyme disease.<sup>2, 3</sup> Failure of initial doxycycline treatment and successful re-treatment has been documented.<sup>4</sup> There is an evidence base to support antibiotic re-treatment of patients with persistent disabling symptoms.<sup>5</sup> A number of complex cases referred on by the LDA helpdesk between 2013 and 2016 for consideration of diagnostic review and antibiotic retreatment resulted in improvement in symptoms and will be presented for discussion. Further research is needed in a clinical setting, into the uncertainties in diagnosis and treatment of Lyme disease.<sup>6</sup>

## References

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4. Dillon R, O'Connell S, Wright S. Lyme disease in the U.K.: clinical and laboratory features and response to treatment. *Clin Med* 2010; 10: 454–457.
5. Fallon BA, Petkova E, Keilp JG, *et al.* A reappraisal of the U.S. Clinical trials of post-treatment lyme disease syndrome. *Open Neurol J* 2012; 6: 79–87.
6. James Lind Alliance. Priority Setting Partnerships. Lyme disease, <http://www.jla.nihr.ac.uk/priority-setting-partnerships/lyme-disease/> (accessed 8 March 2017).

## Declaration of Interest

I am a Trustee of the charity Lyme Disease Action. I work on a voluntary basis in the role of Medical Director.

My husband developed Lyme disease in 2009 and until 2011 I was his registered carer. This lived experience has influenced my perception of the challenges facing clinicians and patients.

## Spots, ticks, fleas & chiggers (Rickettsial diseases worldwide)

Dr Laura Nabarro, University College London Hospital

This talk will attempt to explain the enormous and confusing topic of rickettsial disease worldwide by initially focusing on the shared features of these infections together with diagnostic and treatment options. It will then discuss the differences between the three main groups of infection - the spotted fevers, the typhus group, and *Orientia tsutsugamushi*, - before illustrating these with some clinical cases.

## Learning points

- Appreciate that rickettsial infections are found worldwide, although many are only found in restricted geographical areas.
- Understand the similarities in the diagnosis and treatment of these infections.
- Recognise the clinical syndromes associated with the spotted fevers and the variation in severity of different infections.

- Comprehend the differing epidemiology of epidemic and endemic (murine) typhus
- Describe the emerging nature of *O. tsutsugamushi* (scrub typhus) in South and South-East Asia, its differential diagnosis and the severe manifestations of infection.

### **Clinical “typhus” cases**

Dr Nick Beeching, Liverpool School of Tropical Medicine

#### **Learning points**

- Most rickettsial infection seen in the UK is in the spotted fever group (*R africae* or *R conorii*) from Africa or scrub typhus from Asia including India etc
- Endemic (murine) typhus is usually milder and probably missed often. Much more cosmopolitan
- Clues apart from travel are fever, headache, malaise, maybe dry cough followed by rash
- Look everywhere (hairline, all nooks and crannies) for eschar
- Also for lymph nodes (may be asymmetrical)
- Rash less common in *R africae*
- Rash may affect palms/soles
- Think about deafness and retinitis (asymptomatic) as bedside clues sometimes
- Clinically may have to consider CCHF if illness severe (eschar very unusual) and appropriate geographical contact (includes S Africa)
- Laboratory clue may be high CRP (compared to dengue etc)
- Molecular tests on eschar swabs & EDTA bloods useful for diagnosis as well as late convalescent serology
- If in doubt give doxycycline

### **Zika and its mimics**

Dr Kate Woods, University College London Hospital

#### **Learning points**

- The history and epidemiology of Zika, its mimics and their vectors
- Clinical differentials – including case vignettes
- Diagnostic challenges
- Where to go to – life after

The history, epidemiology and transmission of Zika Virus will be presented drawing parallels and contrasts with its main mimics Dengue and Chikungunya. Clinical cases will be used to highlight the important differentials to be borne in mind when considering Zika Infection. There will be a discussion of some of the diagnostic challenges of Zika and associated arboviruses, including a brief discussion of challenges for diagnostics of emerging infections and lessons learned from the Zika epidemic.

#### **References**

1. Simpson, D. Zika virus infection in man. *Trans Roy Soc Trop Med Hyg* 1964 [https://doi.org/10.1016/0035-9203\(64\)90201-9](https://doi.org/10.1016/0035-9203(64)90201-9)
2. Mayer *et al.* The emergence of arthropod-borne viral diseases: A global prospective on dengue, chikungunya and zika fevers. *Acta Tropica* 2017; 166:155–163.
3. Lessler *et al.* Assessing the global threat from Zika Virus. *Science* 353 aaf8160. 2016.

4. Faye O, Freire CCM, Iamarino A, Faye O, de Oliveira JVC, Diallo M, *et al.* Molecular Evolution of Zika Virus during Its Emergence in the 20<sup>th</sup> Century. *PLoS Negl Trop Dis* 8(1): 2014; e2636. doi:10.1371/journal.pntd.0002636
5. Christofferson RC. Zika Virus Emergence and Expansion: Lessons Learned from Dengue and Chikungunya May Not Provide All the Answers. *Am. J. Trop. Med. Hyg.* 95(1), 2016; pp15-18.
6. In Press Journal of Infection 2017 Clinical features of patients with Zika and dengue virus co-infection in Singapore. <http://dx.doi.org/10.1016/j.jinf.2017.03.007>

## Clinical problems with Zika infection

Dr Emma Aarons

### Learning points

- Zika virus infection is typically a (mild) *rash* illness, rather than a febrile illness
- The widely promulgated “80% of infections are asymptomatic” is probably an overestimate
- Diverse evidence indicates that ZIKV infection is a trigger for Guillain Barre Syndrome and a cause of congenital neurological abnormalities, including microcephaly
- Published reports of other severe sequelae (such as meningoencephalitis or uveitis) or of fatal infection are remarkably rare
- Clinical features of severe Congenital Zika Syndrome are microcephaly with partial skull collapse, occipital protuberance, redundant scalp skin and arthrogryposis
- To learn about full spectrum of congenital Zika disease, we will need to follow up women with documented Zika virus infection during pregnancy and study their fetuses/neonates prospectively

The spectrum of clinical presentation of Zika virus infection and its sequelae will be presented. The features of congenital Zika syndrome will be highlighted. The uncertainty about the risk of a fetus being affected following maternal infection will be discussed.

### References

1. de Laval *et al.* Lancet 2016. Prospective Zika virus disease cohort: systematic screening. [http://dx.doi.org/10.1016/S0140-6736\(16\)31429-5](http://dx.doi.org/10.1016/S0140-6736(16)31429-5)
2. Krauer, F *et al.* PLOS Medicine 2017. Zika Virus Infection as a Cause of Congenital Brain Abnormalities and Guillain Barre Syndrome: Systematic Review. <http://dx.doi.org/10.1371/journal.pmed.1002203>
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4. Moore, CA *et al.* Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians. JAMA Pediatrics 2016. doi:10.1001/jamapediatrics.2016.3982
5. Honein, MA *et al.* Birth Defects among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy. JAMA 2016. <http://jamanetwork.com/journals/jama/fullarticle/2593702>
6. Paz-Bailey, G *et al.* Persistence of Zika Virus in Body Fluids — Preliminary Report. NEJM 2017. <http://www.nejm.org/doi/full/10.1056/NEJMoa1613108#t=article>

## Casebook of infected animal bites

Dr Marina Morgan

### Learning points

- Never use flucloxacillin or erythromycin alone for animal bites
- Animal's normal mouth flora is key - watery animals have different bacteria
- 'spider bites' are not always due to spiders.....
- Cat bites much more infectious than dog bites
- Human bites need managing like inoculation injuries ...
- Don't suture limb bites if possible

I will cover several types of animal bite, the ideal management and antimicrobial Rx- covering what to do and what one should NOT do

## References

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3. Pippiers *et al.* Acute generalized exanthematous pustulosis following a *Loxosceles* spider bite in Great Britain. *British Journal of Dermatology* 2009 161, pp187–218
4. Wang *et al* *Streptobacillus moniliformis* septic arthritis: a clinical entity distinct from rat-bite fever? *BMC Infectious Diseases* 2007, 7:56
5. Gaston *et al.* Hand and Wrist Animal bites to the hand 2010
6. Tregale *et al.* Cercopithecine herpesvirus 1 risk in a child bitten by a bonnet macaque monkey *J Emerg Med* 2011 41, e89–e90

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## Venomous bites (covering snakes and arthropods)

Professor David Warrell, University of Oxford

### Learning points

- Bites by UK's indigenous adder (*Vipera berus*) are potentially dangerous. Appropriate early "ViperaTAB" antivenom treatment reduces morbidity.
- Many species of exotic snakes are kept in UK, legally and illegally, in zoos and in people's homes. DoH holds antivenoms to cover envenoming by most species.
- In UK, bites by false black widow (*Steatoda*) spiders can cause mild neurotoxic symptoms but exotic species can cause severe neurotoxicity (*Latrodectus* – black/brown widows) or local necrosis (*Loxosceles* – brown recluse).
- In UK, stings by yellow-tailed scorpions (*Euscorpis flavicaudis*) are harmless, but exotic species produce excruciatingly painful and sometimes dangerous envenoming.
- Stings by Hymenopteran insects (bees and wasps) precipitate anaphylaxis in sensitised people. Self-administered adrenaline and long-term desensitisation are effective.
- Toxbase<sup>R</sup> <https://www.toxbase.org/> for health professionals only, provides online and personalised expert advice by 'phone

Venomous animals inhabit most parts of the world, especially tropical countries. England, Scotland and Wales have only one species of indigenous venomous snake (adder *Vipera berus*) and a few mildly venomous arthropods. However, anaphylaxis from bee and wasp stings is relatively common.

Prevention is based on knowledge of habits and favourite habitats of local venomous fauna, wearing adequate shoes and clothing, using a light at night, sleeping off the ground, being trained in first-aid and avoiding handling or provoking these animals.

Snake bites: traditional first-aid methods; including tourniquets, electric shock, local incisions, suction, instillation of chemicals and cryotherapy are useless and damaging. Reassurance, immobilisation, application of a pressure-pad over the bite wound and rapid transport to medical care are recommended. Antivenom, the only specific antidote, is given intravenously. Adrenaline must be available to treat anaphylactic reactions.

Insect stings: bees, wasps, and hornets (ants in Australia and the Americas) commonly sensitise people to venom-anaphylaxis. Some hairy caterpillars and moths cause rashes after contact.

Scorpion stings: scorpions fluoresce in ultra-violet light. The agonizing local pain is best palliated by local anaesthetic ring-block of the stung digit. Systemic envenoming by exotic species requires antivenom and ancillary cardiorespiratory support.

Spider bites: spiders are unjustly blamed for a variety of chronic necrotic and granulomatous skin lesions. In the Western Hemisphere, *Loxosceles* (recluse) spider bites can cause severe local necrosis. Neurotoxic araneism is caused by black and brown widow spiders (*Latrodectus*), South American wandering (*Phoneutria*) and Australian funnel-web (*Atrax*, *Hadronyche*) spiders.

## References

1. Warrell DA. Treatment of bites by adders and exotic venomous snakes. *BMJ*. 2005 Nov 26;331(7527):1244–1247.
2. Warrell DA. Commissioned article: management of exotic snakebites. *QJM*. 2009 Sep;102(9):593–601.
3. Warrell DA. Venomous bites, stings, and poisoning. *Infect Dis Clin North Am*. 2012 Jun;26(2):207–223.
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