A talk with Dr Carsten Nicolaus MD PhD on:

The Latest Advances & Improvements in the Understanding & Treatment of Tick-borne Diseases

13th April 2021 – 4:00pm GMT
In support of Lyme Disease UK
To understand ticks, and their relationship with animals, including man, we have to go back to the beginning of time.

We have to understand how clever they are, how they have evolved to survive, and why this in turn makes them one of man’s most challenging adversaries.
The evolution of ticks began more than 100 million years ago

The tick belongs to the group Arthropodas
Ticks parasitised feathered dinosaurs as revealed in Cretaceous amber fossils

Abstract
Ticks are currently among the most prevalent blood-feeding ectoparasites, but their feeding habits and hosts in deep time have long remained speculative. Here, we report direct and indirect evidence in 99 million-year-old Cretaceous amber showing that hard ticks and ticks of the extinct new family Deinocrotonidae fed on blood from feathered dinosaurs, non-avian or avian excluding crown-group birds. A *Cornulipalpata* humanicus hard tick is entangled in a pennaceous feather. Two deinocrotonids described as *Deinocroton draculi* gen. et sp. nov. have specialised setae from dermestid beetle larvae (hastites) attached to their bodies, likely indicating cohabitation in a feathered dinosaur nest. A third conspecific specimen is blood-engorged, its anatomical features suggesting that deinocrotonids fed rapidly to engorgement and had multiple gonotrophic cycles. These findings provide insight into early tick evolution and ecology, and shed light on poorly known arthropod-vertebrate interactions and potential disease transmission during the Mesozoic.
Human Evolutionary Path

10 million years

8 – 4 million years

circa 300,000 years

But remember – ticks have been around over 100 million years!
They have had MUCH longer to adapt to the world and mammals than we have to them.
Ötzi - also called ‘the Iceman’

Ötzi – ‘the Iceman’, is the natural mummy of a man who lived between 3400 and 3100 BCE.

Discovered September 1991 in the Ötztal Alps (hence the nickname "Ötzi") on the border between Austria and Italy.
In the beginning.....

1883 Dr. Alfred Buchwald described a skin lesion he named Acrodermatitis chronica atrophicans (ACA)
In the beginning.....

• **1909** Arvid Afzelius described an expanding ring-like skin rash, later named Erythema Chronicum Migrans.

• **1920s**, Garin and Bujadoux described a patient with meningoencephalitis, painful sensory radiculitis, and erythema migrans following a tick bite, which they attributed to a spirochetal infection.

• By the mid **1930s**, neurologic manifestations associated with *Ixodes* ticks (also known as deer ticks) were recognized and were known as tick-borne meningoencephalitis.

• In the **1940s**, Bannwarth described several cases of chronic lymphocytic meningitis and polyradiculoneuritis, some of which were accompanied by erythematous skin lesions.

• **1990** dermatologist Dr. Bernard Berger (Southampton, NY), recognizing that the rash is not chronic, renamed it Erythema Migrans, or simply, “EM”.

![Ring-like skin rash](image)
Lyme Disease History

- **1975**
  - Alan Steere, MD
  - JRA epidemic in Lyme CT

- **1991**
  - Willy Burgdorfer, Ph.D.
  - Borrelia Burgdorferi, first isolated
How about the Guidelines regarding chronic stages?

<table>
<thead>
<tr>
<th>LD interpretations of the literature</th>
<th>IDSA</th>
<th>NICE</th>
<th>ILADS</th>
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<tbody>
<tr>
<td>Chronic Symptoms</td>
<td>Common</td>
<td>No</td>
<td>Common</td>
</tr>
<tr>
<td>Active infection</td>
<td>No</td>
<td>No</td>
<td>Common</td>
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Tick-borne Diseases (TBD) - most commonly seen obstacles to healing

• In the average patient, multiple chronic infections are often present but these are rarely taken into consideration by standard healthcare systems*

• **Bacterial infections**
  - Borrelia species (Borrelia sensu latu, Borrelia Relapsing fever group), Bartonella, Ehrlichia / Anaplasma, Rickettsia, Chlamydia species, Mycoplasma species, Tularemia, Brucella

• **Parasitic infections**
  - Babesia species, Piroplasma, Toxoplasma

• **Fungal infections**
  - Candida etc.

• **Viruses**
  - EBV, Cytomegalo, Coxsackie, HHV6, Herpes

* In 90% of patients based on statistics from the BCA-lab & BCA-clinic database.
Tick-borne Diseases (TBD) - most commonly seen obstacles to healing

Different bacterial escape & survival strategies:

• **Pleomorphism**
  - Different forms (states) of the same bacterium

• **Intracellular Bacteria**
  - Borrelia & co-infections are all intracellular infections

• **Persisters**
  - Stationary Phase/ Biofilm or Microcolony

  • Recent scientific research has identified Borrelia and Bartonella as a “bacteria”, similar to TB & Leprosy persister cells.

  • Persisters are a small fraction of dormant bacterial cells that survive lethal antibiotics and can regrow.

References:
*Persisters, persistent infections and the Ying Yang model, Ying Zangh; Emerging Microbes and Infections(2014)3, e3;doi:10/ emi2014.3
Most commonly seen obstacles to healing

**Immune system deficiency is a common presentation in patients:**

- **Immunoglobulin & subclass deficiencies**
  - Some pathologies in patients could explain the onset of severe symptoms and complaints.

- **Immune overactivation**
  - Elevated autoimmune and inflammatory markers

**GI issues:**

- **Disruption of the microbiome, SIBO, Leaky gut, Gluten & other sensitivities**
  - Lactose, Fructose etc.

- **Enzyme deficiencies**
  - Pancreas etc.

- **Nutritional deficiencies**
  - Lack absorption of essential nutrients from food
Many Lyme patients also need to deal with:

- Mould
- MCS & Detoxification
  - Environmental toxins, genetic predispositions e.g. polymorphism (MTHFR)
- Mitochondrial Dysfunction
- Resistant POTS / Dysautonomia
- Sleep disorders
  - Disrupted sleep patterns, insomnia, hypersomnia
- Endocrine disorders
- Pain syndromes
Killing Biofilms is essential to get a good treatment outcome!
Killing Biofilms is essential to get a good treatment outcome!

It is this form that is part of the bacteria’s evolutionary strategy to survive that we have not acknowledged until recently.

We need to educate the medical world that it is these biofilms that are responsible for causing ‘chronic’ and ‘long-term’ Lyme.
Interestingly, viruses can create biofilms as well, and it is suggested that ‘long Covid’ might be due to the same phenomena as with Lyme – biofilms and persister cells that are still living within the organism.
Biofilm Busters

How might a biofilm explain the persistence of Lyme?

- Forming a biofilm is a very effective protective mechanism, and bacteria encased in a biofilm are **highly resistant to antibiotics** (up to 10,000-fold).
- Antibiotic treatment is often not effective against cells protected in a biofilm.
- Unfortunately, cells within a biofilm can return to their free-living form and escape to form new biofilms and/or colonize new tissues.
- Since antibiotics can’t be continuously given to a patient, there really isn’t anything to stop these bacteria cells from spreading the disease.
- It’s really a vicious cycle.

The biofilm is an evolutionary tactic by the bacteria to hide when under threat (by the immune system, antibiotics etc.) and emerge and recolonize when it is safe to do so.
Key Points in the Treatment of Lyme Disease and Co-infections

- There has been paradigm shift in patient diagnostics, treatment & care

- No more “one size fits all treatment” approach for patients
  - A tailored medical approach is needed to improve patient care based on many influences that contribute to these chronic infections and associated health conditions.

- Treatment should be holistic, patient centred, and personalised
My personal learnings and observations of the complexity of TBD after seeing my first cases in 1990

1. How important it is to listen carefully to my patients and to examine them thoroughly. This has taught me to pay attention to the particular patterns of "non-specific symptoms" and to classify them correctly at the same time as identifying and confirming the “safe” signs of Lyme or other TBD (EM, ACA, Lyme arthritis, Facial paresis and Chronic Fatigue, etc.).

2. To question the general guidelines (IDSA, NICE, and other national ones) that say that TBD and especially Lyme is easy to diagnose and treat and that chronic courses are very rare.

3. To recognize that not everything is only Lyme disease and that the co-infections also play a crucial role in patient management care.

4. To question standard routine diagnostics ("two-tier testing") and to continually seek out and utilise new diagnostic tests (LTT, Elispot, i-Spot, FISH, Multiplex PCR, etc.)

5. To begin treatment with more complex treatment protocols, especially combinations of different antibiotic classes under the aspect of pleomorphism, intracellular occurrence of TBD and stationary phases ("persisters") of TBD.

6. To introduce “anti-malarias” like Artemisia annua, Hydroxychloroquine, etc in addition to other antimicrobials - not only to treat the parasitic TBD like Babesiosis, but even more to enhance the efficacy of the antibiotics in the intracellular environment.
My personal learnings and observations of the complexity of TBD after seeing my first cases in 1990

7. Chronic infections, especially with intracellular pathogens, almost always require long-term antimicrobial treatment, in most cases a minimum of 4 weeks.

8. IV antibiotics can definitely accelerate the response to therapy, improve tolerance and shorten the duration of therapy.

9. To offer additional support to my patients with pre- and probiotics to reduce GI side effects.

10. That holistic treatment concepts and multi-model therapeutic approaches shorten the overall length of therapy and improve the therapeutic outcome.

11. That the use of tuberculostatics such as rifampicin and others in addition to the classical combinations of macrolides and tetracyclines to increases the therapeutic effect.

12. To systematically detect, analyze and treat additional disease conditions too.
My personal learnings and observations of the complexity of TBD after seeing my first cases in 1990

There are 3 main treatment methods and it appears that for the chronic patient, the Conventional + Alternative route when used in combination yields the best results. (data collected from BCA-clinic)

<table>
<thead>
<tr>
<th>Method</th>
<th>What is it called?</th>
<th>What is it made up of?</th>
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<tbody>
<tr>
<td>1</td>
<td>Conventional Treatment Protocol</td>
<td>Usually prescription medication such as: Antibiotics, Antimalarials, anti-parasitic</td>
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<tr>
<td>2</td>
<td>Alternative Treatment Protocol</td>
<td>Herbal medication to kill Lyme &amp; co-infections as well as detox, reduce inflammation, help with cellular regeneration and energy metabolism and much more. Also includes supportive supplements such as vitamins &amp; other nutrients to help strengthen and support your body and immune system.</td>
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<tr>
<td>3</td>
<td>Mixed Treatment Protocol</td>
<td>Combining the use of Conventional antibiotics etc AND Alternative herbal/supportive treatment to both kill the Lyme/co-infections &amp; support the body’s healing and regeneration.</td>
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*Please note* that the treatment that is right for ‘you’ the patient depends entirely on how chronic your case is, what your co-infections are, and how you respond to various treatments.
Hope for the future: A summary of the most recent advances in the last 5 years

- The new generation of T-cellular testing (“i-spot testing technique”)
  - An excellent diagnostic tool but more useful and recommendable for monitoring purposes to improve the therapeutical outcome.

- More and routiniously use of Next Generation Sequencing (NGS) methods to improve diagnostics and also treatment.

- Introduction of new treatment options beside the antibiotics like Disulfiram & Methylene Blue medications
  - Medications developed for other indications and medical purposes which seem to have extraordinary antimicrobial efficacy.

- Development and improvement of other treatment options for chronic infections and the accompanying health conditions like Peptides, SOT, stem cell treatment, hyperthermia, etc.

- The growth globally of charities and organisations supporting patients worldwide, advocating for change and awareness
  - LDUK @11K members, France Lyme – the only support patients have, Finland, Germany, USA etc.
In conclusion:

Even after 30 years, there is always something new to discover.

Awareness of the disease is on the increase, and with this comes (eventually) wider acceptance by the medical field.

The complexity & methodology of diagnostic testing is constantly improving.

Treatment options are constantly increasing and improving.

The therapeutical outcome for patients is getting better year-by-year.

Patient success rates have constantly improved over the past 30 years.

It **IS** possible to be free of Lyme symptoms and lead a healthy and full life.
In conclusion:

BUT FURTHER PROGRESS CAN ONLY BE ACHIEVED IF:

- We raise more awareness for TBD and improve medical training for healthcare professionals!

  Long-term treatment can be provided for patients. This is not a quick fix.

  Treating a Lyme patient requires a lot of time, patience, information gathering and often a lot of medication, this takes time and there is no quick win or solution.

  We need to set a gold-standard for testing and treatment that holds the Lyme world accountable.

  Too often there are practitioners/doctors who prescribe incorrect or insufficient treatment to patients.

  This wastes the patient’s time, their hope, and their money with them often getting caught in a never-ending cycle of various treatment trials as they hop from one treatment recommendation to the next.
Thank you for your attention today.

Dr Carsten Nicolaus, MD PhD

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Questions?
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