A pilot study on ……

"Granulated cellular structures" and other abnormal microscopy findings in blood from chronically ill patients ..

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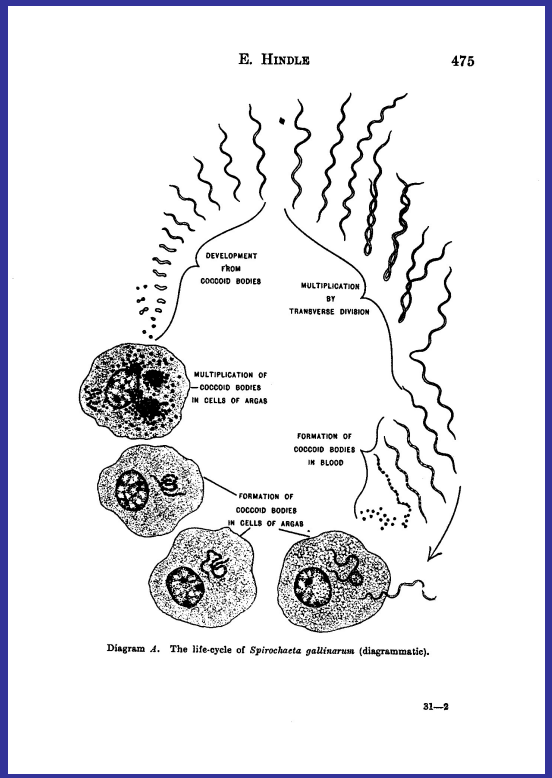
LymeRICK: http://LymeRICK.net
ILADS (International Lyme and Associated Diseases Society): www.ilads.org

(NOTE in this updated version typo-errors and links (light blue) has been adjusted after the LymeRICK website had moved!)

Spirochaetes

- old important observations giving us hints ….

- 1911 Balfour
- 1912 Hindle →
- 1914 Nicolle & Blanc
- 1914, 1915 Sergent & Foley
- 1916 Fantham
- 1918 Leishman
- 1948 Hampp
- 1957 Pashoud



Persistence is the keyword …

- The old guys had to look at the same in the microscope for up to 2-3 weeks or longer to get nearly the whole picture ….
- Less persistent observers could NOT confirm their observations, thus discarded the findings as not true
- Others did see the granulation, but thought that this process was a die-off phenomenon and that granules were just DEAD degradation products, a logical assumption when looking at samples in a FIXED STATE …
- **Result:** the complex spirochaetal lifecycle theory was considered wrong and the findings were NOT mentioned in any of the Microbiology teaching books …
- **Today I will SHOW you that the 'granules' aren't dead, but ALIVE and MOVING !**

Borrelia burgdorferi

- newer important observations supporting the old …

- Several published works demonstrate that Borrelia goes intracellular, and that intracellular location protects Borrelia against antibiotics that do not cross cell walls well like penicillin and ceftriaxon (Georgilis 1992, Brouqui 1996).
- Alternative cystic / spheroblast / L-form of Borrelia forms whenever the environment is hostile: presence of antibiotics (more), antibodies (Aberer), lack of nutrients (Alban, Brorson), in spinal fluid or distilled water (Brorson) – from which they can revert to spirochaetal form again, if given a more suitable growth environment.
  See pictorial of alternate forms in LymeRICK.
- Intra-peritoneal injection of cystic forms of *Borrelia garinii* in mice resulted in infection and SPIROCHAETES were found in tissues (Gruntar).

Timing is important …

- cyclical symptoms explained, importance of symptom diary …

- *Relapsing fever Borrelia* : historic works showed that spirochaetes are present in the blood only during the weekly relapses, but the blood is just as infective in between the symptomatic relapses, when no spirochaetes were present !

  Symptoms ~ immune reaction to spirochaetes.

- *Borrelia burgdorferi* : is also a **CYCLICAL, RELAPSING DISEASE** - explained by the difference in growth velocity found between young (~9 days) and old (3-4 weeks) cysts (Brorson).

This may become clinically obvious when the patient keep a **detailed, graduated symptom diary**:

- a weekly (8-10 days) symptom cycle, seen in early / very active Borreliosis, and
- a monthly cycle, may develop spontaneously during late, chronic infection and is commonly seen during long-term antibiotic treatment of Borreliosis, as described by Burrascano in his guidelines (see ILADS guidelines).

Timing is important …

- implications for antibiotic treatment

- All antibiotics interfere with active metabolic processes like protein synthesis, DNA synthesis or formation of the cell wall !
- **Dormant, inactive bacteria can't be hit by antibiotics, because the metabolic processes are NOT active !**
- High doses of antibiotics is usually needed in order to reach 'privileged locations' - like tendons, inner eye, vertebral disc, CNS - in sufficient concentration to kill or suppress the growth of bacteria.
- Borrelia can apparently persist and stay dormant for YEARS in such 'privileged locations', from where they can recur later and cause verified relapses of Borreliosis – despite even long-term antibiotic treatment !
- Antibiotics taken during inactive periods can be a total waste, toxic for the host and more expensive … while IME a high dose PULSE antibiotic treatment (oral) taken on start of and during each flare, can both maintain the improvement gained, and will usually in time lead to increasing intervals between flares = longer lasting remission …
- **Pulse antibiotic therapy - minimal treatment, minimal toxicity, minimal cost – but perhaps increased risk of resistance - unless COMBINATION therapy is given ?**

The Paradox …

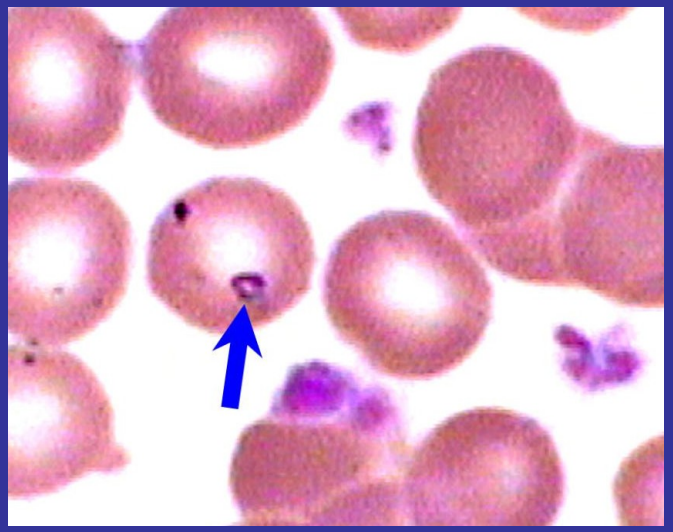
- That an infectious agent, which relies mainly on transmission from one mammalian host to the other via a bloodsucking vector, but which only rarely can be found visible in blood in its spirochaetal form at relatively long intervals (8-10 days), is explained by the so-called equally virulent and infective 'invisible stage' described by some of the old guys, but for the fact that IT IS NOT INVISIBLE !
- Look for 'granulated cellular structures' which looks like the structures that react positively with Borrelia antibody in the DIRECT fluorescent antibody stain ~ **RIBb©** done by Bowen RTI.
- Videomicroscopy like Viljanen (http://www.utu.fi/research/tic/viljanen) showing darkfield microscopy of 'tube phagocytosis' of spirocaete form of *Borrelia burgdorferi;* note the in darkfield bright moving 'granules' ….
- Video1 - Video2 (WMV) by Marie Kroun, showing moving 'granules' and 'granulated cellular structures'
  (Note: made with Windows Movie Maker, only plays with **Windows Media Player** !)

33 patients - SUMMARY of most important findings:

- All had typical CHRONIC Borreliosis symptoms, i.e. often recurrent influenza-like infectious symptoms as sign of cyclical infectious activity, usually a weekly or monthly pattern ~ the inclusion criteria when no history or serology pointing to TBI
- All had POSITIVE results with Bowen RTIs (www.bowen.org) DIRECT FLOURESCENT ANTIBODY STAIN ~ RIBb(c)
- All had similar 'granulated cellular structures' in their blood as patient#18 filmed in the two videos ...
- Age span 5-55 years, mean 35 years; 1/3 acquired CHRONIC illness in their best age before age 40.
- 95% were sick for more than 1 year, disease duration span: 5 months to 43 years!
- 36% were SERONEGATIVE for Borrelia flagella antibodies despite typical Borreliosis history and symptoms and positive RIBb-test; 27% of patients with EM as debut symptom had no reported flagella antibodies. (41% of EM culture+ stayed Borrelia S-anti-Fla neg.)

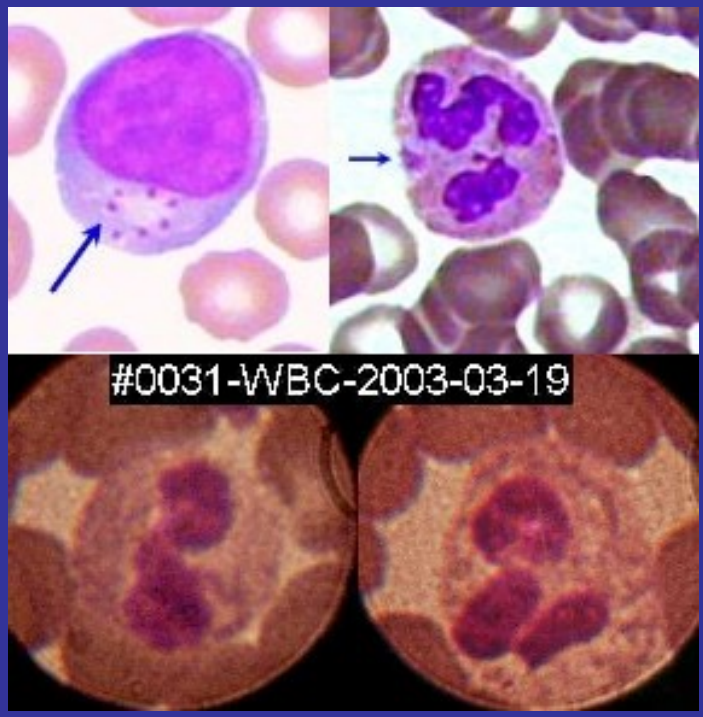
10 of 33 chronically ill patients had BABESIA-like ring forms INSIDE their RBC ..

- INTRACELLULAR **RING-FORMS** in RBC is NEVER a NORMAL finding!
- Babesia resemble Malaria
  Protracted disease more and worse symptoms in Borrelia + Babesia co-infected patients i.e. slow and suboptimal response to antibiotics like amoxicillin and doxycycline, much better response to anti-protozoa drugs like quinine atovaquone, metronidazole …
- Combination therapy necessary to avoid development of antibiotic resistance
- Persistence of Babesia
  (free download after reg. @ NEJM)
  is a well-known problem, exemplified by transmission by transfusion of blood from apparently healthy donors!



9 of 33 chronically ill patients had abnormal inclusions in their WBCs ..

- The microscopist must know what normal WBC and blasts, as well as what all the parasites and bacteria look like in the microscope !
  WBCs are phagocytic cells that ingest all sort of microbes !
  Thus, a dark blue dot in the cytoplasm is not always 'Ehrlichia', can represent many bacteria – give risk of over diagnosing, if specific IF-stain (recommended by CDC) isn't used!
  Few project patients had the typical MORULAE of EHRLICHIA i.e. bacteria inside a 'vacuole´
- Spirochaetes is usually extracellular, but there is much evidence that Spirochaetes can survive intracellularly, also in immune cells .. protected from the action of cell wall antibiotics !!!



Chronic TBI was often misdiagnosed as ME/CFS, fibromyalgia or other *syndrome diagnoses* of unknown aetiology!

- 10 females & 2 males=12 patients ~ 36% of all the 33 project patients described here were diagnosed with ME/CFS or fibromyalgia, despite **5 of these had positive Borrelia-serology and/or tick bite and/or EM in their history pointing to probable chronic TBI as cause of their disease!**
- ALL CFS-patients without TBI-history or positive Borrelia-serology displayed the - for persistent active borreliosis - so very characteristic cyclical – weekly or monthly – symptom pattern on which they were enrolled in project!
- 3 patients were diagnosed with CFS, without being evaluated for other relevant causes like chronic infections, that according to the diagnosis criteria for ME/CFS must be excluded !!!

Somatizing, anxiety ….

- Many patients were told – without proper evaluation for disease: it's just stress, psychosomatic, atypical depression, age, hormonal …
- Many patients had asked in the conventional medical system for **- but WERE REFUSED !!! - ANTIGEN TESTING for persistent Borreliosis and possible co-infections**, despite this was possible to do and such tests were well indicated based on the patients history and chronic recurrent disease, especially after temporary successful antibiotic treatment for recognized Borreliosis and then relapse!
  Many doctors OUTRULED or UNDIAGNOSED a previous - EM-based - diagnosis of Borreliosis, when serology came out negative, despite there are plenty of published cases of CULTURE VERIFIED RELAPSES OF SERONEGATIVE BORRELIOSIS – even some that DEVELOPED SERONEGATIVITY despite culture-verified persistent borreliosis **WHY are not all chronic TBI patients examined and treated as thorough as that patient ?**
- Illiterate doctors said many wrong and undocumented things to patients, which the patients could look up in PubMed and see was false. **WHY don't doctors offer more true knowledge and professional medical conduct to these knowledge seeking 'help-yourself' type patients? Are doctors too stressed to CARE for their patients?**
- **WHY ARE MANY DOCTORS SO AFRAID OF ACKNOWLEDGING THE EXISTENCE OF CHRONIC TICKBORNE INFECTIONS?**

Conclusion & Recommendation:

- The patients with chronic infections – whether tick-borne or not - deserve the doctors best services, ALWAYS ! – because it is worth while to test, diagnose and treat these infections, though NOT ALWAYS EASY TO HANDLE.
- The infective agent is apparently formed inside the 'cysts' from breakdown of spirochaetes into 'granules', which can move around both inside and outside the cellular structures!
  All MDs – who own a simple Microscope - should TRY to do WET BLOOD DROP MICROSCOPY on patients where Borreliosis is suspected from history, symptom-diary and other test-results.
- When such 'granulated cellular structures' are found, Bowen RTIs RIBb test will usually confirm the diagnosis of Borrelia burgdorferi ANTIGEN in the blood.
  Look for the green apple, instead of the snake in Paradise !
- Judging from the pilot project, the number and severity of symptoms seem to correlate well with number of 'granulated cellular structures' in the blood – but yet few patients have been followed and only for 1-2 years, so this is subject of further study in a 5 year prospective project.

A MILLION THANKs to the patients, without whom this ongoing study would not be possible to conduct ….

Note – before criticizing what was NOT done in this study of multiple relevant tests – you need to know that:

- All expenses of this pilot study was paid solely by the courageous patients, who was willing to search new paths, offer me their trust and money and willing to make a thorough diary, despite many of them were long term sick, were low on 'energy', 'brainfogged' and had lost much income !!!
- **The number and type of tests performed were therefore limited to what individual patients could afford to pay for or what was already done before they came to see me …**
- There is SURE much need for further investigations, like extended serology testing for all known TBIs, PCR-studies … why do the commonly used PCR for Borrelia flagella gene NOT find the 'granules'? – is the genetic material in 'cysts' in form of RNA - as mentioned by Brorson's - not DNA or …..????
- **FURTHER STUDIES WILL NEED MONEY, therefore please make donations to the patients support groups in your country, which will support further scientific studies of these chronic infections !**