Bowen test project
Excel Symptom Diary
Case#49 & Case#50

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LymeRICK (Eng.): http://LymeRICK.net
Project side (Danish) : http://kroun.ulmarweb.dk
ILADS : http://ILADS.org
1999 a patient made a homemade diary with point scores, that when summed up showed cyclically peaking symptom about every 3 weeks. Curve lost in hard disk crash.

2001-2003 pilot project #1-#33; all patients were requested to make a list of all their symptoms and score from day to day using a personal scale. About 1/3 did make a homemade diary. More showed cyclical symptom pattern, and more showed improvement during antibiotic treatment!

However, due to different symptoms scored and different scales used - it was impossible for me to compare patients, and besides it was a huge job to enter all the scores manually into a chart in order to draw curves and get overview over the course.

I HAD TO INVENT A DIARY THAT COULD DRAW CURVES INSTANTANEOUSLY – along as scores are entered.

I HAD TO DEFINE A COMMON USEFUL SCALE, where KEY INTEGER SCORES where explained in WORDS, which humans relate to much better than to NUMBERS, which computer needs for the curves …

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>normal condition, normal function</td>
</tr>
<tr>
<td>1</td>
<td>slightly abnormal, slightly reduced function</td>
</tr>
<tr>
<td>2</td>
<td>moderately abnormal, moderately reduced function</td>
</tr>
<tr>
<td>3</td>
<td>highly abnormal, highly reduced function</td>
</tr>
</tbody>
</table>

[3+ can be used, if a patient get worse than we thought possible]

Is there one or more CYCLEs?

Follow intervention:
- score 1-3 months pre-treatment, during treatment and 3 months post-treatment
- compare and read result on curves

Total score shows disability level:
- 60 point ~ score maximal 3 point on 20 symptoms, the patient is practically unable to function!
Case #49 - Key points / history

- 43-year old man, previously healthy and fit, high level racing cyclist
- **1999 tickbite** on right shoulder, developed a discrete red rash at the bite site, but did not contact doctor, thus no antibiotic treatment.
- 2000 sudden 12 kg unexplained weight gain
- 2000 elevated alkaline phosphatase, fluctuating with activity
- 2001/05 fatigue and abdominal pain, chest X-ray i.a.
- 2001/06 severe headache for 10 days, and "something" with his eyes; phadiatop allergy panel i.a.
- .... Long interval no notes ....
- 2005/11 leg pain, chest pain, increased BP, ECG left hypertrophy
- **2006/01 brain infarct in left frontal lobe, 4 x 3 x 2 cm**
- **2006/01 NEUROBORRELIOSIS**: spinal fluid: cell count 77; spinal protein slightly increased; Borrelia IgG positive in CSF & SERUM; serum Borrelia-IgM slightly positive (despite many years duration since tickbite and probable EM)
  - **yet the neurologist describe borreliosis as coincidental, not cause!**
  - see a short reference list on Borrelia associated with vasculitis and infarct on slide 7
- **2006/01 IV ceftriaxone 2g daily for 10 days; ”FANTASTIC effect”**
- **2006/03 increasing symptoms, his GP starts PENICILLIN 1.5 MIO x 3**
- 2006/04 considered improved; still positive spinal borrelia titer, however, serum borrelia titer has turned negative
  - ”no need to believe you still have active borreliosis”
- **2006/05/31 stops penicillin and starts Excel diary & enters project as #49**
Symptom diary shows gradually increasing symptoms after stopping penicillin

2006/07/04 Q-RIBb titer 1:128

2006/07/12 is denied IV antibiotic treatment in hospital ID; starts metronidazol, later azithromycin => visible improvement on total curve

2006/10/24 (3 months) improved, less GCS, but small moving extracellular filamentous structures. Rash still present, but vague: 0049-20061024-skin.jpg

2006/12 skin biopsy from rash: perivascular lymphocytic inflammation with a few plasma cells, compatible with ACA, but not alone diagnostic; this after 5 mo. of M+A and clinically improved!

Hospital paper states that nothing had helped the patient BUT for 1. IV ceftriaxone Tx. – however, this in contradicted by the total symptom score pattern showing clear improvement of more than 50% symptom reduction after 3 mo. Tx. (did the pt. not show the diary to the DRs?)

2007/04 IV ceftriaxone 2g daily for 2 weeks, doxycycline 100 mg x 2 for 3 weeks. He has continued doxycycline via GP.
Case 49# shapshots & videos from microscopy of buffy-coat

0049-20061024
170 Mb, 16 min

0049-0070305
58 Mb, 8 min
Improvement during treatment on totalscore:
Before Tx: 35-40, fluctuating; long "second herx", then after 4 mo Tx. Reduced to ~ 10, stabile; IV ceftriaxone: down to 5, stabile
CEREBRAL VASCULITIS & BRAIN INFARCT associated with Borrelia infection (just a few …)

- Defer et al. Neuroradiology 1993; 35(7): 529-31. **Lyme disease presenting as a stroke in the vertebrobasilar territory:** MRI
- Keil et al. Nervenarzt 1997 Apr; 68(4): 339-41. [**Vasculitis course of neuroborreliosis with thalamic infarct**][German]
- May et al. Stroke 1990 Aug; 21(8): 1232-5. **Stroke in neuroborreliosis.** (case + review of 11 literature cases)
- Oksi et al. Brain. 1996 Dec;119 (Pt 6):2143-54. **Inflammatory brain changes in Lyme borreliosis.** A report on three patients and review of literature. From abstract: "The objective of this study was evaluation of neuropathological, microbiological, and magnetic resonance imaging (MRI) findings in three patients with the Borrelia burgdorferi infection and neurological disease from whom brain tissue specimens were available. Perivascular or vasculitic lymphocytic inflammation was detected in all specimens. ..... We conclude that cerebral lymphocytic vasculitis and multifocal encephalitis may be associated with B. burgdorferi infection. The presence of B. burgdorferi DNA in tissue samples from areas with inflammatory changes indicates that direct invasion of B. burgdorferi may be the pathogenetic mechanism for focal encephalitis in LNB."
Case#50: Key points / history

- 37 year old formerly very fit and sports active business man, travelling all over the world
- 2005/04 he develops respiratory symptoms and muscle aches after exposure to formaline fumes in a fabric in China. The area is known as being the cradle of many epidemics like influenza, SARS, corono virus
- Many mosquito bites while in China, no malaria prophylaxis taken (low risk area)
- Many known tickbites in previous history, but he had not been symptomatic after this before
- Never seen any rashes of 5 cm in diameter or bigger
- 2005/05 and later: SERUM antibodies (FL-ELISA) for Borrelia burgdorferi negative
Slight increase in body temperature (sub-febrilia) accompanied fluctuating muscle aches – suggested an ”influenza-like” illness

Concurrent with the bouts of muscle aches, Creatin Kinase (CK) values were elevated (even over 4000), measured several times, however spontaneous decline occurred in between the pain attacks; the CK rises were probably NOT provoked by extensive training, because CK value increased also, when the patient had not done any training!

MYOSITIS has been found associated with infections like Borrelia (PubMed), and also many virus infections like influenza, parvovirus, coxsackie - and though suggested – titer results for the these viruses are missing in his laboratory report …

……. a rheumatologist concludes ”possible somatoform disorder” and dismisses the patient?!

He tries glyco-nutrients and feel some improvement - BUT the patients condition gradually worsens

He has to go on long term sickleave
Despite the previous negative serum borrelia titer, the patient still suspect possible borreliosis, due to symptoms alike (list on next slide)

Pt. already knows that a negative SERUM borrelia titer does not 100% outrule active borreliosis, as 6 of 12 culture verified late cases of Borreliosis were missed by the FL-ELISA test [J. Clin. Microbiol. 1995; 33(9): 2260-4 PDF]

2006/03 a neurologist agrees and refers him to hospital for a lumbar puncture and measure of spinal antibodies for borrelia

Lumbar puncture was done, resulting in normal spinal cell count and protein

The patient is told the results of all tests were normal

2006/06 he asks for the Q-RIBb test, that only I’m doing in Denmark - thus he starts Excel symptom diary and enrolls in my long term research project, and send me all the necessary previous data for my review;

However, I miss the exact measures from the spinal and serum borrelia titer and ask the patient to ask for these again from the hospital

It turns out that his spinal and serum borrelia titer was not done after all – spinal fluid was saved in a freezer ???!!!
Case#50: Symptom list

- Fatigue
- Weight loss (3 kg / 5 days) despite normal intake of food and drink
- Temperature measures now normal between 36.4 og 37.5 (rectal) [no longer subfebrilia]
- Muscle aches – acid feeling, stiffness
- Marked neck pain and stiffness (loss of muscle volumen)
- Backpain suggesting possible disc prolapse, but normal scan outrules this
- Sore tenderpoint (neck, knee)
- Blood pressure slightly higher than before
- Pulse swings, palpitations
- Short of breath
- Sinus problems
- Dizziness / problems with balance
- Numbness, decreased sensibility in fingers
- Prickling feeling in skin, change in temperature of skin (cold/warm)
- Stomach aches and increased number of defecations (up to 4, previously 1 daily)
- Periodic "drop attacks"
- Decreased vision contrast and night vision
- Increased sensibility to light and sound
- Problems with short-term memory, attention and orientation
- **Symptoms cycle with worsenings about every 30 days**
FALSE statements made by senior doctors in hospital ....

"you can’t have borrelia, because your serum antibody is negative"

"spinal antibody index can not be calculated, because your serum value is zero"

a. this patient's borrelia seronegative status was known before the lumbar puncture, i.e. **IF the first statement was really true, the hospital did an un-necessary, painful invasive procedure, that is not without risk**; the patient did suffer from post-lumbar puncture headache, and developed more severe neurosymptoms after the puncture ...

b. The second statement is formally correct, however, it is simple logic, that when serum antibody titer is zero, then a calculation of the organism specific antibody index for borrelia, is NOT warranted, really!
   **If a positive measure in CSF and negative in SERUM, those antibodies in CSF must all have been produced intrathecally!**

c. **Negative SERUM borrelia antibody does not exclude neuroborrellosis**
   [Tidsskr Nor Laegeforen 2001; 121: 2008–11.]
   "Fourteen of 25 (56%) patients had positive Borrelia burgdorferi-IgM and IgG titres in cerebrospinal fluid despite negative Borrelia serology test in serum"]
FALSE statements often made by senior doctors in Danish hospitals....

“*It is not possible to see spirochetes / borrelia in the blood by microscopy*”

“*It is not possible to see spirochetes / borrelia in phase contrast microscopy, only in dark-field microscopy*”

=>

“*What MK has found and videotaped in your blood by phase contrast microscopy, can not be borrelia / spirochetes – therefore antibiotic treatment is not warranted in your case*”
These doctors had apparently not read / seen ....

DeLamater et al. Studies on the life cycle of spirochetes. 
VIII Summary and comparison of observations on various organisms. 
J Invest Dermatol 1951; 16:231-56
By means of the phase contrast microscope the following general story of development of spirochetes appears to be consistent in those organisms studied. The conditions governing the occurrence of the forms observed and reported are under study. In the current presentation representative plates from several of these organisms will be presented in attempting to present the total picture as it has been observed up to the present time. ... Authors describe and document by photos multiplication of spirochaetes by:
* Transverse fission.
* Production of gemmae as a means of vegetative reproduction.
* The production of multispirochetal cysts by the aggregation of organisms.
* The production of multispirochetal cysts by internal reorganization.

MAGNIFICATION X4850

Andy Wright’s high resolution video clips presented on http://LymeRICK.net
Shot with the Bradford Microscope (magnification up to X10000)
Andy shifts between phase contrast and dark field modes many times, thus show us, that it is possible to see the same structures equally well in boths modes, if the magnification is just high enough!

DIGITAL MAGNIFICATION by computer is possible!
Borrelia spirochaetes in BLOOD and tissue - as seen in the microscope.
The original Bb B31 after culture for one year in the laboratory

**Atypical forms of Bbss / B31:**

- **cyst**
  - (= "granulated cellular structure"
  - = L-form
  - = spheroblast .... )

- **granula**

- **spirochaetes**

All structures reacted well with added specific antibodies towards Borrelia burgdorferi!

IFA is not a new method, dates back to 1940-ies!
Specific immune stain for Borrelia burgdorferi

Method of Bb-specific antibody production described by KPL:
Affinity purified polyclonal antibody to Borrelia burgdorferi made in Goat and labeled with fluorescein isothiocyanate (FITC). Isolated from a serum pool of goats immunized with heat killed whole cells of Borrelia burgdorferi. The antibody is highly specific for Borrelia burgdorferi. Cross reactivity to Borrelia hermsii, Borrelia coriaceae, and Borrelia anserina has been minimized through extensive affinity adsorption.

  Quantification of reactivity by titration, result visualized in the microscope and documented by pictures of both immune stain and phase contrast of same structure

- **2007 new lab. name: Central Florida Research Inc.**
  "NEW" test – is still based on same immune stain but quantification is done by computer counting (flowcytometry)
  CFR and the flowcytometry IF-test for Bb has been approved by: CLIA, Florida state, Medicare ....
Case#50 – treatment course

Current Tx does NOT work well, but I can’t give IV and the hospital won’t trial treat 😞
Snapshots and videomicroscopy of #50s blood (BC)

0050-20061025
90 Mb, 8 min
Doxy 100 mg x 2: no certain effect
Doxy 200 mg x 2: improvement from 40 to 15 point

0050-20070411
98 Mb, 9 min
2007/02 Worsening despite cont. Doxy
FREE SPIROCHETEs?
Shift to metronidazole plus azithromycin, with minimal pos. effect 😔
Case#50 – treatment course

Current Tx does NOT work well, but I can’t give IV and the hospital won’t trial treat 😞
Invasion and cytopathic killing of human lymphocytes by spirochetes causing Lyme disease. 
In vitro study. Spirochetes selectively attach to, enter and burst immune cells

"The macrophage is a known reservoir for a number of infectious agents, and is therefore a likely candidate site for persistence of Borrelia burgdorferi, the Lyme spirochete."
"Moreover, we can reculture spirochetes from macrophages after infection."
"Persistence of spirochetes within macrophages provides a possible pathogenetic mechanism for chronic or recurrent Lyme disease in man."

Bone Marrow as a Source for Borrelia burgdorferi DNA.
"Patients may lose their immune response over time or it may be abrogated by antimicrobial therapy. These case reports describe patients with chronic Lyme disease and a reactive bone marrow polymerase chain reaction (PCR). After appropriate and aggressive treatment, specific DNA may persist in sequestered sites such as bone marrow."

Lymphocyte apoptosis co-cultured with Borrelia burgdorferi.
"Our data suggest that spirochetes were able to induce apoptosis on lymphocytes; the phenomenon appears associated with number of spirochetes, incubation time and the release of IL-10 in co-cultures. Moreover apoptosis was probably Fas-mediated and the cells involved were prevalently CD4."

Could the “granulated cellular structures” (GCS) - i.e. cellular structures with lots of moving granules inside - perhaps be MACROPHAGES, that have ingested Borrelia spirochetes, that are broken down – just like drawn by Hindle 1912?

My long term study indicate that the more “GCS” found, the more sick the patient feels - now documented by diary+ repeated videos of these pts. blood during course of treatment, both when successful (#49), and during relapse (#50).
Some of my favourite CITATIONS:

...... my work, which I've done for a long time, was not pursued in order to gain the praise I now enjoy, but chiefly from a craving after knowledge, which I notice resides in me more than in most other men. And therewithal, whenever I found out anything remarkable, I have thought it my duty to put down my discovery on paper, so that all ingenious people might be informed thereof.

Antony van Leeuwenhoek.
Letter of June 12, 1716

...... following a routine examination and fixed treatment prescriptions will never allow the recognition of new patterns.

Butler
1991: 94

...... The acceptance of a new scientific truth does not depend on the convincing of the skeptics. Rather it results when the critics eventually die off, and a new generation arises, that is familiar with the idea from the beginning.

Max Planck,
Nobel prize-winning physicist
Questions?

I hope you found the presentation interesting and perhaps inspiring?

Thank you very much for your attention.