From Cellular Anoxemia caused by the presence of Rickettsiae to CFS

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Topics

- Rickettsial Infection
- Distribution
- Material and Methods
- Treatment
- Measurement of Progress
- Discussion
Rickettsial Infection

- Discovered in 1909
- Initially epidemic forms
- Latterly slow evolving forms
- Distribution
- Vascular pathology
- A constellation of Diseases

Rickettsial infection was discovered in 1909, when Ricketts saw and described the germ that causes RMSF in man. Ricketts, as well as another scientist, Prowazek, contracted Typhus and died.

1. The epidemic forms of Rickettsiae were described by Zinsser in his classic book “Rats, Lice and History”, in which he contends that soldiers have rarely won wars. Typhus and other infectious diseases have decided the outcome of more military campaigns than Caesar, Hannibal, Napoleon and all generals in history. Depending on the outcome for each warring faction, either the epidemics were blamed for defeat, or the generals were credited with victory. It has contaminated an estimated 25 million Russians, causing 3 million deaths during the 1st World War.

2. Nowadays, following on from these historical memories, there are forms less virulent, evolving slowly, but able to induce vascular and neurological pathologies.

3. Rickettsiae are found in ticks, lice, fleas, mites, meat, milk, stools and dust. From the entry into the skin, the lungs, conjunctives, and the digestive mucosa, Rickettsiae spread via the bloodstream to infect vascular endothelium. These organisms grow and multiply by binary fission in and only in the cytoplasm of the host cell until the number of Rickettsiae is so great that the cell bursts, releasing hundreds of them. This invasion will impair or paralyse the vascular function, acting like a sponge between blood and organs. They will enlarge the endothelial cells of small vessels with partial or complete occlusion of the vascular lumen. They are known for long survival in various organs and lymphatic tissue. According to which vessel they invade, they might display an amazing constellation of diseases:
   - CFS, Fibromyalgia, where they cause a cellular anoxemia
   - Cardio-vascular diseases
   - Neurological diseases (from acute encephalitis to MS, epilepsy etc) Abdominal diseases (appendicitis, coeliac disease and others)
   - Ocular diseases (uveitis, retinal angiopathy, optic nevritis sometimes a long time after a general infection)
   - AutoImmune diseases

Rickettsiae release into the bloodstream, angiotropic endotoxins, producing inflammations, allergies and demyelinisation (H Perron).
**Distribution of Rickettsiae**

- They are:
  - humidity and dryness resistant
  - stayers:
    - virulent for 60 days in milk
    - 4 months in sand
    - 6 months in meat
    - 7 - 9 months in cotton
  - spread by rodents and birds and by modern air traffic
- Fish and oysters share the disease

Rickettsiae:
- are resistant to humidity and to dryness
- will stay virulent for:
  - 60 days in milk
  - 4 months in sand
  - 6 months in meat
  - 7 - 9 months in cotton

They are spread by rodents and birds. Through the centuries, bird migration has been responsible for changing the geographical distribution of disease - but this is nothing compared to the effect of the explosion of these diseases due to the cocktail effect created by distribution through global air traffic.

Equally the transport of insects compared to the import and export of livestock - as in the case of the importation of 10,000 parrots from Paraguay to Belgium when some 2,000 died, leaving the virus well and alive behind them (identified by JB Jadin as Neo-Rickettsia Bedsonia).

This world distribution does not include Antarctica, where they do not survive.

Fish also share this disease, as Erlichioses is, according to breeders, a common problem. They have been found in oysters by Deltreil.
Material and Methods

3,600 patients presented with CFS, Fibromyalgia, RA, Depression, MS diagnosed with CRI

CRI established by Giroud M-A test:
- R. Prowazeki – R. Mooseri – R. Conori
- Coxiella Burnetti – Neo Rickettsia Chlamydiae

Important:
- High reading = High antibodies
- -ve reading = Low immune system
- +ve tests found without symptoms (26%)

3,600 patients presented with CFS, Fibromyalgia, RA, depression and MS have been diagnosed as suffering from Chronic Rickettsial Infection (CRI) after eliminating other diseases as a cause (diabetes, cancer etc.).

The majority of my patients report a flu-like infection, with often an elevated temperature and severe headaches. This lasts for a few days, disappears or reoccurs, and then leaves them with a chronic condition of CFS, Fibromyalgia etc. as mentioned above.

Diagnosis of CRI is established by Giroud's Micro-Agglutination test against five strains of Rickettsiae:
R. Prowazeki: the epidemic type of Typhus
R. Mooseri, which is endemic
R. Conori, which belongs to the spotted fever group
Coxiella Burnetti, which is well known as Q Fever. It has 2 phases; Phase II is pathogenic
- Neo Rickettsia Chlamydiae which has an affinity for uterine mucosa, and will be the cause of many abortions.

Important Points:
A high reading means a high serological level of antibodies - a negative reading in endemic areas reflects the poverty of the immune system.
Agglutination happens or does not - therefore there is no possibility of personal interpretation. Test quality depends on Antigen quality.
Positive tests can be found in people who display no symptoms (Giroud, Jadin; 26% according to Drancourt).
Material and Methods (Biology)

Giroud not the only tool.

Blood tests:
- LFT
- Iron
- Thyroid AB - 28% of cases
- CRP, RF, ANF, WR - 53% of cases
- Mycoplasma

However, the Micro-Agglutination test of Giroud is not our only tool to establish the diagnosis of Rickettsial infections. We find the following blood tests most relevant:

LFT: the hepatotoxicity of Rickettsiae has been reported as early as 1937 by Derrick in Q Fever followed by many others - Giroud, Lenette, Legaq, Brezina, Perron, Kelly, Raoult, etc. In these cases, Tetracyclines are improving or normalising liver function.

Iron study (50% of abnormalities corrected with Tetracyclines only and when necessary with a short course of iron supplement).

Thyroid AB rather than TFT, although the TFT show abnormalities in 3% of patients, the thyroid AB are elevated in 28% of cases and improve or normalise rapidly with treatment.

CRP, RF, ANF, WR was positive in 53% of patients, and also improved with treatment and often normalised.

Mycoplasma, first classified as Rickettsia, is now considered to be an independent entity.
Material and Methods (Symptoms)

- Tiredness
- Headaches, retroorbital and temporal
- Myalgia
- Arthralgia migrating
- Loss of balance
- Vision abnormalities
- Raynaud syndrome
- Nausea
- Recurrent sore throat
- Memory and concentration deficit
- Chest pain, palpitations
- Sweats, low grade fever
- Bruising
- Psychological and neurological disorders
Material and Methods (Physical Examination)

- Inflamed throat
- Multiple adenopathies
- Heart abnormalities; vascular and valvular
- RIF tenderness - Chlamydiae in Appendix
The treatment consists of 7 to 12 days per month of a specific Tetracycline. The monthly treatment aims to follow the Rickettsial development in the cell.

**A high dosage** is required with the limitation of:

- **Safety:** Goodman et al highlights irreversible hepatotoxicity in intravenous administration only. Our experience was that when liver functions were normal to start with, they stay normal. If they were abnormal, they will improve during treatment and generally return to normal. Cases of fatty acid depots (as shown by liver scan, before and after 6 months to 1 year of treatment) have disappeared (1 MS, 4 ME). This confirms the fact that Rickettsiae are more hepatotoxic than Tetracyclines.

- **Tolerance:** The gastric intolerance will be successfully prevented by using a gastric pump inhibitor during and if necessary before and after the administration of the Tetracyclines. The tolerance of the treatment is directly related to the **Herxheimer** reaction, which is a reactivation of old symptoms and/or exacerbation of present symptoms, that occurs on antibiotherapy. Its presence has a very important diagnosis and prognosis value. They might or might not be parallel to a serological reactivation. It will fade with the number of treatments received. When very severe, the **Herxheimer** is treated with Probenecid.

The Tetracyclines are **alternated** because: A patient is frequently contaminated by many strains of Rickettsiae and different Rickettsiae have different sensitivity to different Tetracyclines, or combinations. A patient might build resistance to each Tetracycline. Patients show individual sensitivity to different Tetracyclines or combinations and there is very often a privileged reaction to a specific treatment.

The Tetracyclines are **combined** with Quinolones, Macrolides or Metronidazole, because Rickettsiae present a wide heterogenicity of susceptibility to different drugs.

The treatment is often **long** due to: The chronicity of the germ, The multiple foci of Rickettsiae and The fact that Rickettsiae have a slow evolution and some foci are dormant, encapsulated and therefore protected from antibiotherapy. Only when they become active can they be treated.

Each treatment will allow the immune system to produce and maintain a proper and efficient level of antibodies. This happens each time the antigen Rickettsiae are released from the cell to the blood stream while on antibiotherapy.

The **length** of the disease should logically imply a **lengthy** treatment. In our experience, this point is **not always true**. Patients, ill for many years, may recover after a **few months** treatment.

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Antimalaria has been found efficient to improve Rheumatoid symptoms and Rheumatoid biological findings (see patients' files).

Adjuvants such as Vitamin B complex and acidobacillus are also used.

Cortisone is avoided as much as possible as it is known to weaken the Immune System in general and also to reactivate the disease in experiments on guinea-pigs. Cortisone has been accused of interfering with the diagnosis of Rickettsia by masking the antibody level.

Exercise is recommended, for 3 reasons:

- Rickettsial infection is a vascular disease and exercise, properly done, will improve the smooth peri-vascular muscle function, as well as develop our biggest muscle, the heart.
- The fact that strains of Rickettsiae grow better in vitro when maintained in a CO2 enriched atmosphere (34).
- The suggestion that Rickettsiae grow best when the metabolism of the host cell is low (38).

Hot baths are important to eliminate toxins via the skin, produced by Rickettsiae antigens when liberated in the bloodstream by antibiotherapy.

Reinfection may obviously occur. Reactivation (called so rather than relapse) may also happen due to the interaction of bacteria, virus, stress, pollution, etc. causing the Rickettsiae forms' change to active from dormant.
Measurement of Progress

Patients seen monthly to judge progress:
- Symptoms
- Activity increase
- Reduction in medication:
- Medical examination
- Biological investigation - back to normal:
  - LFT
  - RF
  - CRP
  - KFT
  - Thyroid antibodies
  - Iron

Assess treatment

Patients - either
- Fast progress - illness mainly Rickettsia
- Slow progress - illness Rickettsia +

Patients are seen monthly to judge progress on their symptoms, activity increase - from bedridden to back to exercise or back to work; - from being treated by painkillers, antidepressants, sedatives, cortisone to none. They are given a medical examination, and a biological investigation to measure the progress back to normal, or nearly so of: LFT - RF -, CRP -, ANF -, KFT -, Thyroid antibodies -, Iron.

Based on the assessment, the treatment is prolonged or stopped. The time period can be 3 months to 2 years; and is 8 months on average. However, as previously mentioned, the length of treatment is not directly correlated to the length of illness:

Therefore patients can be divided into 2 categories:
1. Fast progress - their illness was mainly Rickettsia
2. Slow progress - their illness was Rickettsia plus other factors.

NEXT SLIDE
"La salute è come un pallone d’aria calda; a volte bisogna rilasciare il peso"
12 years ago, one of my friends became unable to walk and was diagnosed as having ME. For 4 years I suggested the diagnosis of Rickettsial Infection, and therefore the Weil-Felix test was performed several times in South Africa, but the results were negative. My friend developed an acute appendicitis. After I removed her appendix, her serum was sent to Prof. JB Jadin in Belgium to test for Rickettsiae, and the result was positive. I treated her with Tetracyclines and 3 weeks later, from being in a wheelchair; she was riding her horse again. I was sceptical. But this case brought me 200 patients and the publicity surrounding an investigation of my methodology by the South African Medical Council brought me several thousand more. Thus I started to focus on the Rickettsial approach.

There are many reasons suggesting the infectious etiology and, more specifically, Rickettsial-like organisms of CFS. Amongst those reasons:

• CFS was first reported in Incline, Nevada in 1984 and developed into epidemic proportions.

• Rocky Mountain Spotted Fever originated from the same place in 1916. The spirochete Borrelia Duttoni, first blamed for causing the recurrent Malgache fever described in the journals written by Drury in 1702 in Madagascar, then by Scheltzin in the Belgian Congo in 1933, by Palakov in Cape Town in 1944, by Heisch in Kenya in 1950.

• Lyme Disease appeared more recently in Lyme, Connecticut in 1975 (Borrelia Burgdorferi). As Lyme Disease is a new name for Malgache Fever, could CFS be a new name for Rickettsial Disease?

All of the above highlights the life of a germ as an individual emerging and disappearing in a wave pattern epidemiologically and historically. Like us, germs have to adapt, producing new variations of themselves, (not new species), that may or may not survive on their own, with or without the help of another germ. This is circumstance-dependent, and these particular circumstances will never reoccur. Some of those variations will acquire specific and consistent characteristics.

This is their 'civilisation'. We only see them when they succeed, and only then do new avenues of investigation open up, while others are abandoned.

A link has been established between Florence Nightingale disease and CFS. The fact that she was working surrounded by lice, fleas and ticks, treating soldiers with wounds and with epidemic typhus during the Crimean war, could be a logical explanation as to why she was terribly tired during the last 2 decades of her life; and possibly has relevance to Gulf War
Lymphocyte studies conducted on sheep with tick-borne diseases, CFS patients and patients with Q Fever endocarditis are showing amazingly similar results.

Coincidentally, the new name suggested in the Lancet for CFS is PQFS (Post Q Fever Syndrome) in April 1996 edition

As mentioned above, during the First World War an estimated 25 million Russians contracted Louse-borne epidemic typhus, resulting in 3 million deaths. Why not before or after? It could suggest that the stress factor reactivates the virulence of Typhus Prowazeki. In the medical history of CFS patients, stress has often been described as the start of the illness.

The symptoms displayed by CFS, Fibromyalgia, RA, and even neurological patients as MS, show the same diversity of symptoms as Rickettsial patients. How many scientists blamed the diversity of symptoms for misleading unprepared practitioners in the diagnosis of chronic Rickettsial infection? That same diversity could have contributed to the delay in recognising CFS. French authors (Giroud, Jadin, Legag) attribute those multiple aspects to a generalised micro-vascular invasion. They widely demonstrated the persistence of Rickettsiae in the vessels. The suggestion here is that the well-known, well-documented entity of Rickettsial disease, showing the same symptoms as the newly arrived CFS, might simply, partially or totally be caused by the same agent.

The last, but not the least reason, is the success rate of the Rickettsial treatment, Tetracycline, applied on CFS, Fibromyalgia etc. patients. Dr Phillippe Bottero on 100 patients, Dr Peter Tableton on 300 patients and myself on a much larger number of patients, maintain an 84% to 96% recovery rate.