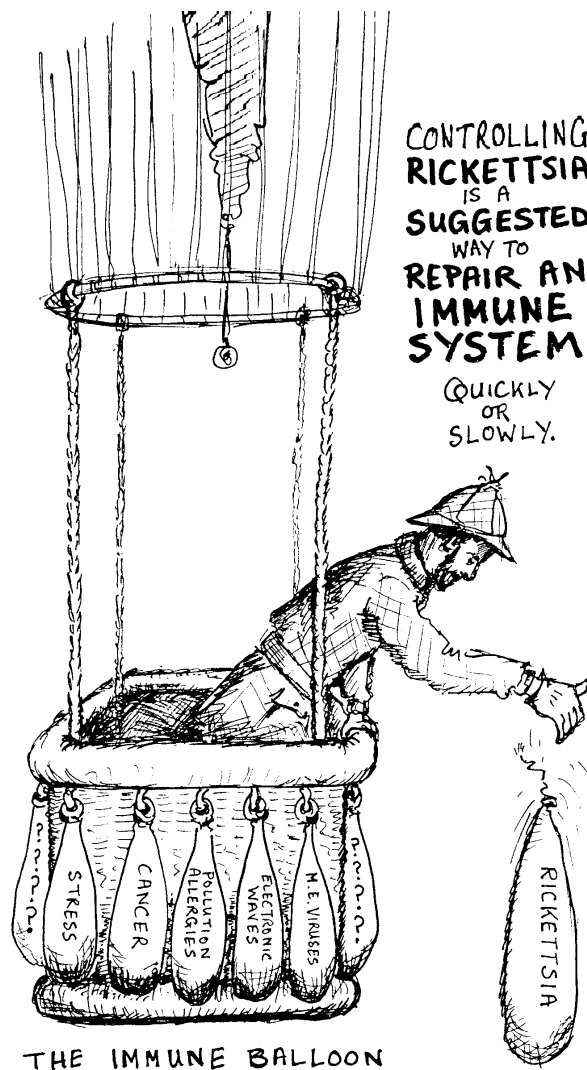


The Rickettsial and Para-Rickettsial Approach of CFS

And Related Disorders

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Health is like a hot air balloon; it is sometimes necessary to get rid of some burdens

ACKNOWLEDGMENTS

Thanks to my father, Prof. JB Jadin, and his Pasteurian colleagues, I have at my disposal an impressive collection of scientific literature.

Thanks to the faith of my numerous patients, I have my illustrated pathology.

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Because of all of the above, I have been able to participate in International CFS World Congresses (Sydney 1998 and 1999, Brussels 1999 and the address to the University of Padua in 1999). This provided me with more insight into CFS-like diseases, and gave me the opportunity to present my clinical evidence in scientific publications.

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The Rickettsial and Para-Rickettsial Approach of CFS, Fibromyalgia, Rheumatic Arthritis, Neurological and Psychological Dysfunction

“ Ceux auxquels nous devons rendre compte de nos travaux, la société, ne nous demandent pas tant de tracer des aperçus généraux que de trouver quelque chose qui soit pratique pour le diagnostique, la prévention et le traitement des maladies”.

CHARLES NICOLLE

PREFACE

Germs on earth are fighting to subsist. We only realise their existence when they enter our lives. To achieve this, like surfers, they take the first wave they can. One wins a thousand dies. Diseases appear and disappear throughout the centuries, producing new variations and mutations of themselves not new species. Here comes a new name for an old disease.

INTRODUCTION

The author, Cécile Jadin, is originally from Belgium, but has been practising in South Africa since 1981. She is a surgeon by profession. In South Africa, in addition to practising as a surgeon, she also assisted her husband in his general practice. For the last 8 years, she has focused on patients presenting with CFS-like symptoms.

This paper presents a summary of her clinical experience linked to her scientific research.

To understand why she took the Rickettsial approach, her background needs to be explained. Her father was Professor JB Jadin, who undertook groundbreaking research on tropical diseases, among them Rickettsial infection, with Professor Paul Giroud in Central Africa, South Africa, the Near East, and in Europe, developing the work started in the Pasteur Institute of Tunis, with Professor Charles Nicolle, who was a disciple of Louis Pasteur. Thus she was familiar with those germs from an early age and her work represents the results of teamwork through the last 100 years.

At the end of 1987, one of her friends became unable to walk and was diagnosed as having CFS. For 4 years Dr. Jadin suggested the diagnosis of Rickettsial Infection, and therefore the Weil-Felix test, the only one then available in South Africa for diagnosis of Rickettsia was performed several times, but the results were negative. The friend developed an acute appendicitis that needed surgery. Afterwards, her serum was sent to Prof. JB Jadin in Belgium to test for Rickettsiae, and the result was positive. Dr. Jadin treated her with Tetracyclines and 3 weeks later she was riding her horse again. Thus Dr. Jadin started to focus on the Rickettsial approach.

RESEARCH

Research on Rickettsioses was originally developed by French, Polish and Russian scientists. They followed Charles Nicolle's (Pasteur Institute, winner of the Nobel Prize for medicine in 1933) hypothesis, which is that occult diseases are a reality and their cohabitation in the same host will lead to the bankruptcy of the immune system. By occult disease Charles Nicolle implies the asymptomatic stage of the disease, where the agent is present in the host, but dormant. The emergence of a virus, bacteria, parasite, stress or pollution can activate this agent, which leads to the symptomatic stage.

An example of this cohabitation is the infant mortality rate described by J.B. Jadin in Central Africa. Neonates diagnosed with malaria and *Coxiella Burnetti* all died as opposed to those with malaria only.

The numerous publications of these authors are unfortunately all in French, so their circulation was limited. They also, as academics, excluded the media. Therefore the real importance of their discovery is still to be made widely known.

RICKETTSIAL DISEASES

Rickettsial infection was discovered in 1909, when Ricketts saw and described the germ that causes Rocky Mountain Spotted Fever (R M S F) in man. Ricketts, as well as another scientist, Prowazek, contracted Typhus and died.

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.

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

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 and this vascular sponge will be the cause of memory loss, and/or muscular weakness and pain,

and/or palpitations, and/or ulcers, depending on its localisation. These organisms 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 a constellation of symptoms; amazingly similar to those presented by the CFS group of patients that may be the origin of a flock of diseases such as:

- CFS, Fibromyalgia, where they cause a cellular Anoxemia.
- Cardio-vascular diseases, (valve replacements, infarctus, high blood pressure).
- Neurological diseases (from acute encephalitis to Multiple Sclerosis (MS), epilepsy etc).
- Abdominal diseases (appendicitis, coeliac disease and others).
- Ocular diseases (uveitis, retinal angiopathy, optic neuritis sometimes a long time after a general infection).
- Auto-Immune diseases (such as Rheumatoid Arthritis, Psoriatic Arthritis, Lupus, Scleroderma, Sjögren Disease).

Some patients will present, simultaneously, or one after the other, many diseases. For example, it is common to see the following association: Rheumatoid Arthritis and Depression; Ocular Disease and heart attacks; Appendicitis and CFS; Hashimoto Disease and high blood pressure. Upon closer scrutiny, it is the same germ causing damage to different organs, either together or consecutively. Alternatively, one patient suffering from ME might develop MS, and one patient presenting with MS, has a greater chance of dying of a heart attack, if not treated. They are different stages of the same disease.

Rickettsiae release into the bloodstream 3 types of endotoxins, which have different effects. All or some of these endotoxins may produce symptoms. First, endocytokines that will cause inflammation and pain; second, neurocytokines that would be the origin of neurological symptoms such as demyelination found in MS patients, and psychological symptoms, such as depression, anxiety, troubled behaviour, sometime even causing attempted suicide and third, allergens producing allergies.

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 Paul Giroud described in 1962, the presence of Rickettsia Piscis; as Erlichia Rickettsi is, according to breeders, a common problem: their advice is for each change of season to treat fishponds with Aquatetra powder (Tetracycline powder manufactured by Aquavet) to prevent this disease. This highlights the fluctuation of virulence of Rickettsiae, according to the seasons. What is called 'The October Suicide' in Africa could be part of the same phenomenon.

Deltreil has reported their presence in oysters, which are commonly eaten raw, and therefore could present a risk of contamination.

The majority of patients in our clinic 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

Diagnosis of Chronic Rickettsial Infection (CRI) is established on **3 cornerstones**:

1 Patients' symptoms

- Tiredness
- Headaches, retro-orbital and temporal, worst after prolonged horizontal position or mental effort
- Myalgia (muscular pain)
- Arthralgia migrating (arthritic pain)
- Loss of balance
- Vision abnormalities
- Raynaud syndrome (cold, painful, often blue extremities, known in South Africa as "Winter hands or feet")
- Nausea
- Recurrent sore throat
- Memory and concentration deficit
- Chest pain, palpitations
- Sweats, low grade fever
- Bruising
- Psychological and neurological disorders

2 The Physical Examination often shows:

- An inflamed throat
- The glands enlarged and painful
- Heart abnormalities (vascular and valvular impact)
- Right Iliac Fossa tenderness (chlamydiae 18 in appendix)

3 The Biological Cornerstone allows us a more specific diagnosis and also helps us to eliminate other diseases as a cause (diabetes, cancer etc). The following checklist has been established over the years in our clinic, finding its best definition with the help of the large number of patients, their various pathologies and the treatment's success on those abnormalities.

This success is demonstrable, not only by the recovered patients feeling well, but by the improvement shown in their blood.

Nevertheless, as time passes, our checklist is subject to modification, in view of improved results.

At this stage we can divide our biological approach into 3 categories:

- 3.1 **Infections**: Rickettsia and Para-Rickettsia organisms such as
- Mycoplasma and Chlamydiae
 - Bilharzia
 - Brucella
 - Toxoplasmoses

For Rickettsial diseases we use the Micro-Agglutination test of Giroud-Jadin against these following five strains:

- 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 Q18 which falls into the Neo-Rickettsia group.

The Antigens of those Rickettsiae are directly collected from the bowels of infected ticks and other arthropods, then mixed in a solution, injected into the peritoneal cavity of guinea pigs, mice, hamsters, rabbits or embryonated eggs to be cultivated.

Before releasing for testing, the solution is attenuated with formol.

3.1.1 **Important Points:**

- 3.1.2 A high reading means a high serological level of antibodies - a negative reading in endemic areas reflects the poverty of the immune system.
- 3.1.3 Agglutination happens or does not - therefore there is no possibility of personal interpretation. Test quality depends on Antigen quality.
- 3.1.4 Quality controls are done with:

- Negative sera
- Pure Antigens, regularly checked to ensure the absence of Auto-Agglutination

3.1.5 Variation of the curve of Antibodies in time reveals the presence of active foci.

3.1.6 If doubtful or negative, in the presence significant symptomatology, the test should be repeated to follow the Antibodies' curve

3.1.7 Tests can give a negative reading if patients are treated with cortisone

3.1.8 Positive tests can be found in people who display no symptoms (Giroud, Jadin; 26% according to Drancourt)

3.1.9 Comparative studies with the Immunofluorescence test and the ELISA test performed by Prof. Jadin and a French Laboratory gave very similar results (NB: The BRUMPT prize of the Pasteur Institute of Paris was awarded to Prof. JB Jadin for this test in October 1997)

3.1.10 The test is currently done upon request in the MATG laboratory in Johannesburg, South Africa; currently for doctors in France, Italy, Germany, Belgium, Australia, South Africa and Zimbabwe

3.2 **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:

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

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

4.2.3 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,

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

4.2.5 Mycoplasma and Chlamydiae, first classified as Rickettsiae, are now considered to be independent entities.

3.3 **The damage produced by those germs in our bodies:**

- Elevated sedimentation rate
- Low white cell count
- Iron deficiency or iron increased
- Abnormal liver function test
- Abnormal Thyroid Function test

3.4 The Abnormalities of the Auto-immune factors produced by those intra-cellular organisms, such as:

- Thyroid Antibodies
- Rheumatoid Factor
- C. Reactive protein
- Antinuclear Factor

After establishing these 3 cornerstones treatment is administered:

TREATMENT

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 CFS). This confirms the fact that Rickettsiae are more hepatotoxic than Tetracyclines.
 - **Tolerance.**
 - a) 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.
 - b) The tolerance of the treatment is directly related to the Herxheimer reaction (HR), 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 HR is treated with Probenecid.
- The Tetracyclines are **alternated** because:

- a) A patient is frequently contaminated by many strains of Rickettsiae and different Rickettsiae have different sensitivity to different Tetracyclines or combinations.
- b) A patient might build resistance to each Tetracycline.
- c) 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 heterogeneity of susceptibility to different drugs.
- The treatment is often **long** due to:
 - a) The chronicity of the germ
 - b) The multiple foci of Rickettsiae
 - c) 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.
 - d) 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 (Legag).
 - e) 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.
- Antimalaria has been found efficient to improve rheumatoid symptoms and rheumatoid biological findings.
- 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.

Chlamydiae have been isolated in the cerebrospinal fluid of **MS** patients (Le Gag, Jadin, 1962, 1986, Sriram, Mitchell 1998) and also in **cardiac valves** (Shor in RSA, 1992).

Equally **Rickettsiae** have been isolated from Mitral and Aortic valves (Grist in Glasgow, 1963, Drancourt in 1990) and are known to cause **Endocarditis and Myocarditis**.

Therefore the use of **cortisone** depressing immune reaction **should be restricted** before infectious investigation.

- **Exercise is recommended**, for the following 3 reasons:

1. Rickettsiae 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.
 2. The fact that strains of Rickettsiae grow better in vitro when maintained in a CO2 enriched atmosphere.
 3. The suggestion that Rickettsiae grow best when the metabolism of the host cell is low.
- Hot baths are important to eliminate toxins via the skin, produced by Rickettsiae antigens when liberated in the bloodstream by antibiotherapy.
 - Regular intake of Multivitamins may be dangerous if we consider the following points:

Germ and their hosts are forming an **Eco-system**. This is the most complex level of organisation in Nature, depending on climate, water, nutrients, and energy.

Due to the gap in our knowledge concerning basic parasite-host interaction, administration of nutritional supplements and diet are a hazardous guess, since it might support the parasite rather than the host (for example: magnesium, glutamate, pyruvate are the principle energy-yielding substrate of Rickettsiae, ethanol kills Rickettsiae in vitro, folic acid supports some leukaemia cells).

- 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' to change to active from dormant.

MEASUREMENT OF PROGRESS

Patients are seen monthly to judge progress on:

1. Symptoms
2. Activity increase (From bedridden to back to exercise or back to work)
3. From being treated by painkillers, antidepressants, sedatives, cortisone to none
4. Medical examination
5. Biological investigation: **from** having:
 - LFT abnormal
 - CRP raised
 - KFT raised
 - Iron abnormal
 - RF raised
 - ANF raised
 - Thyroid antibodies raised

back to normal, or nearly so

Based on this assessment, the treatment is prolonged or stopped (3 months to 2 years: 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.

CONCLUSION

Apart from the radical changes wrought in most of the patients individually, I also would like to appeal for the recognition of CFS as a real disease and to emphasise the role Rickettsial infection plays in this multi-factorial situation. The importance of this role lies in the direct availability of diagnosis and treatment for Rickettsia (unlike viruses, which cannot yet be controlled by medication). The huge socio-economical problem created by this disease could be solved if it were recognised by insurance companies, and diagnosed and treated by medical doctors, as soon as the first symptoms appear.

Furthermore, In the presence of CFS, Fibromyalgia, Auto-immune diseases, Heart diseases, MS, Depression, the screening for **Rickettsial-like infections** might be a valuable tool for treatment. Even Systematic Giemsa or Machiavello stain of removed tissue (appendix, valves, tonsils, placenta of aborted foetus) as done for heartwater disease in cattle brains could improve diagnosis.



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