

The Rickettsial Approach
Dr. CL Jadin

**The Rickettsial Approach and treatment of patients presenting with
CFS, Fibromyalgia, Rheumatoid Arthritis and Neurological
Dysfunction.**

**Mainly Conference
February 1999**

CL Jadin MD MBBCh

Republic of South Africa

The Rickettsial Approach and treatment of patients presenting with CFS, Fibromyalgia, Rheumatoid Arthritis and Neurological Dysfunction.....	1
Original Research	2
Rickettsia and CFS	3
Transmission of Rickettsiae	4
Patients and Diagnosis	5
Symptoms	7
Treatment	7
Measurement of Progress	9
Appendix 1: <u>CFS - Rickettsial Infection: Sources of References</u>	11

The Rickettsial Approach

Dr. CL Jadin

Introduction

The author, Cécile Jadin, is originally from Belgium, but has been practising in South Africa for the last 17 years. 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 7 years, she has focused on the subject of Rickettsia and her approach has naturally been that of a clinician, and it is in this context that the paper is written.

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.

12 years ago, one of her friends became unable to walk and was diagnosed as having ME. For 4 years Dr. Jadin suggested the diagnosis of Rickettsial Infection, and therefore the Weil-Felix test was performed several times in South Africa, but the results were negative. The friend developed an acute appendicitis. After Dr. Jadin removed her appendix, 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. Dr. Jadin was sceptical. But this case brought her 200 patients and the publicity surrounding an investigation of her methodology by the South African Medical Council brought her several thousand more. Thus Dr. Jadin started to focus on the Rickettsial approach.

Original 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 (8). By occult disease Charles Nicolle implies the asymptomatic stage of the disease, where the agent is present in the host, but dormant (3). The emergence of a virus, bacteria, 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 (20).

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.

The Rickettsial Approach
Dr. CL Jadin

Rickettsia and CFS

The fairly recently recognised entity of CFS gives us a perfect opportunity to try the etiological route to understand this disease. Along this route we will automatically enter other medical fields, inviting us to consider an infectious etiology in cardiology (4,5,9,11,12), in psychiatry (3,17), in neurology (3,29) and in rheumatology (28), rather than describing the symptoms and gathering them into syndromes (20, 40).

Obviously one germ can cause many diseases depending on a selective topicality for one or more particular tissues as well as one disease can be caused by different germs alone or simultaneously. Therefore we would like to concentrate on the causative agent, rather than on the name of, and the criteria to classify, the diseases.

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

1. Consider the following :

- CFS was first reported in Incline, Nevada in 1984 (1) and developed into epidemic proportions.
- Rocky Mountain Spotted Fever originated from the same place in 1916 (9,29).
- The spirochete *Borrelia Duttoni*, first blamed for causing the recurrent Malgache fever described in the journals written by Drury in 1702 (24) in Madagascar, then by Scheltz in the Belgian Congo in 1933, by Palakov in Cape Town in 1944, by Heisch in Kenya in 1950.
- Lyme Disease appeared (or reappeared?) more recently in Lyme, Connecticut in 1975 (*Borrelia Burgdorferi*) (25).

Could these be new names for old diseases?

All of the above highlights the life of a germ as an individual emerging and disappearing in a wave pattern epidemically 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 that will allow them to survive. 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.

1. A link has been established between Florence Nightingale disease and CFS (21). 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 illnesses (13). Zinsser has developed the same concept in his classic book "Rats, Lice and History". He contends:

"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

The Rickettsial Approach Dr. CL Jadin

for defeat, or the generals were credited with victory." (2). More examples of this phenomenon were reported by JB Jadin (29).

2. Lymphocyte studies conducted on sheep with tick-borne diseases (14), CFS patients (15,16), and patients with Q Fever endocarditis (11) are showing amazingly similar results.
3. Coincidentally, the new name suggested in the Lancet for CFS is PQFS (Post Q Fever Syndrome) in April 1996 edition (22).
4. 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 (2, 3, 9). In the medical history of CFS patients, stress has often been described as the start of the illness.
5. 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 (30)? That same diversity could have contributed to the delay in recognising CFS. French authors (Giroud, Jadin, Legag) attribute those multiple aspects to a generalized micro-vascular invasion. They widely demonstrated the persistence of Rickettsiae in the vessels (4), (18). 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.
6. The last, but not the least reason, is the success rate of the Rickettsia treatment, Tetracycline, applied on CFS, Fibromyalgia, Depression and MS etc. patients. Dr Phillippe Bottero on 100 patients since 1981, Dr Peter Tarbleton on 300 patients in 1993 in South Africa(17) and myself on a much larger number of patients, maintain an 84% - to 96% recovery rate.

Transmission of Rickettsiae

Rickettsiae are transmitted by arthropods (36), except for Q Fever, which does not really need vectors;

- they are resistant to humidity and to dryness
- they will stay virulent for 60 days in milk
- 4 months in sand
- 6 months in meat
- 7 - 9 months in cotton (4).

They are spread by rodents and birds. Through the centuries, bird migration has been responsible for changing the geographical distribution of disease (27) - 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 (26).

Equally the transport of insects compared to the import and export of livestock - as in the case of the import of 10,000 parrots from Paraguay to Belgium when some 2,000 died, leaving the virus well and alive behind them (27), (identified by my father as Neo-Rickettsia Bedsonia).

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

The Rickettsial Approach Dr. CL Jadin

Fish also share this disease, as Erlichiosis is, according to breeders, a common problem (Psichi Rickettsia Salmoni, first described in Chile) (31).

Patients and Diagnosis

3,400 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 falls into the Neo-Rickettsia group (18)

Important Points:

- a) A high reading means a high serological level of antibodies - a negative reading in endemic areas reflects the poverty of the immune system (24).
- b) Agglutination happens or does not - therefore there is no possibility of personal interpretation. Test quality depends on Antigen quality (3).
- c) Positive tests can be found in people who display no symptoms (Giroud, Jadin (18); 26% according to Drancourt (39)).

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 (19, 29), followed by many others - Giroud, Lenette, Legag, Brezina, Perron, Kelly, Raoult, etc. In these cases, Tetracyclines are improving or normalizing liver function (6).
- 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, (39) and also improved with treatment and often normalised.
- Mycoplasma (only researched after the Manly conference, February 1998).

The Rickettsial Approach
Dr. CL Jadin

The Rickettsial Approach

Dr. CL Jadin

Symptoms

Patients' symptoms most commonly exhibited are:

- Tiredness (4,5)
- Headaches, retroorbital and temporal, worst after prolonged horizontal position or mental effort (4),H
- Myalgia (3)
- Arthralgia migrating (2,3,5)
- Loss of balance (29)
- Vision abnormalities (3,29)
- Raynaud syndrome (18)
- Nausea (8,9,18)
- Recurrent sore throat (23)
- Memory and concentration deficit (4).
- Chest pain, palpitations (8,12, 18)
- Sweats, low grade fever (4)
- Bruising (4)
- Psychological and neurological disorders(4,5,18,29,30)

We find quite a valuable guideline in the physical examination, which often shows

- An inflamed throat and multiple adenopathies, reflecting the selective topicality of Rickettsiae to endothelial tissue
- Heart abnormalities (vascular (4,12,30) and valvular impact (2, 39))
- RIF tenderness (chlamydiae 18 in appendix (23))

Treatment

After establishing these 3 cornerstones Symptoms

Physical examination

Blood tests

treatment is administered:

- Guided by our predecessors, (Giroud, Jadin, Legag etc.)
- Refined by our contemporaries, (Bottero and Raoul)
- And by my own daily, private lessons (each patient is one).

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.

1. A high dosage is required (4,5) with the limitation of:

- **Safety** (32) Goodman et al (33) 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.**
 - 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 (4, 6, 26, 37), 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 (4). 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.

1. The Tetracyclines are alternated because:

The Rickettsial Approach
Dr. CL Jadin

- a) A patient is frequently contaminated by many strains of Rickettsiae (5) and different Rickettsiae have different sensitivity to different Tetracyclines or combinations. (4).
- b) A patient might build resistance to each Tetracycline (4, 17).
- c) Patients show individual sensitivity to different Tetracyclines or combinations and there is very often a privileged reaction to a specific treatment (6).
3. The Tetracyclines are combined with Quinolones, Macrolides or Metronidazole (7), because Rickettsiae present a wide heterogeneity of susceptibility to different drugs (4).
4. The treatment is often long due to :
 - a) The chronicity of the germ (4)
 - b) The multiple foci of Rickettsiae (18)
 - 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 (5).
 - 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) (4).
 - 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.
3. Antimalaria has been found efficient to improve Rheumatoid symptoms and Rheumatoid biological findings (see patients' files). Christopher Columbus knew it in the 15th century, as he gave tree bark containing quinine to his crew to prevent malaria and also mysterious body pains. The Imperial army of Queen Victoria did the same and so was born Indian Tonic water.
4. Adjuvants such as Vitamin B complex and acidobacillus are also used.
5. Cortisone is avoided as much as possible as it is known to weaken the Immune System in general (3) and also to reactivate the disease in experiments on guinea-pigs (39). Cortisone has been accused of interfering with the diagnosis of Rickettsia by masking the antibody level (4).
6. Exercise is recommended, for the following 3 reasons:
 - Rickettsiae is a vascular disease and exercise, properly done, will improve the smooth peri-vascular muscle function, as well as develop the most important 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).
7. Hot baths are important to eliminate toxins via the skin, produced by Rickettsiae antigens when liberated in the bloodstream by antibiotherapy.
8. 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 (35).

The Rickettsial Approach
Dr. CL Jadin

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
- CRP raised
- KFT raised
- Iron
- 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:

The Rickettsial Approach
Dr. CL Jadin

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 (20).

"La santé est comme une mongolfière: il faut parfois lâcher du lest"

Health is like a hot air balloon. You have to get rid of excess burdens to keep it in the air. Rickettsia is the easiest one to lose



The Rickettsial Approach
Dr. CL Jadin

Appendix 1: CFS - Rickettsial Infection: Sources of References

	References		Authors	
<u>1</u>	CFS in Incline Village	1991	Mauff & Gon RSA	
<u>2</u>	Annals New York Academy of Sciences	1990		Preface
<u>3</u>	Acta Mediterranea di Patologia. Infectiva e Tropicale.	1984 Vol 3 1986 Vol 5 1987 Vol 6 no 3	JB Jadin, Ph. Bottero	P213
<u>4</u>	Bulletin Societé de Pathologie Exotique	1963	J. Gear Monteiro S. Nicolau J.G.Bernard N.R.Grist A. MasBernard Roche	P588 P680 P691-714 P758-793 P684-687 P714-724 P724-740
<u>5</u>	Clinique de la Résidence du Parc	1986		
	MS		P. Le Gag	
	Relationship between protozoa, virus & bacteria		J.B. Jadin	
	Psychopathies		Ph. Bottero	
	Buerger Disease		C. Bourde / Delanoï	
	Dermatology		Aymard	
<u>6</u>	Extrait Bull. Acad. Nat. Médecine	Vol 158 N° 1	P. Giroud & J. Jadin	
<u>7</u>	European Journal of Epidemiology	1991	D. Raoult	P276
<u>8</u>	Academie Royale des Sciences d'Outre Mer	1963 N° 6	J.B. Jadin	P1128-1129
<u>9</u>	Ann. Soc. Belge Med. Tropic. : Au Sujet des Maladies Rickettsiennes	1962 Vol 3	J. Jadin	P321
<u>10</u>	Infectious Diseases and Medical Microbiology	2nd Ed.	Braude	P810-814
<u>11</u>	Arch. Int. Med.: Chronic Q Fever	March 8 1993 Vol 153	T. Brouqui et al.	P.643
<u>12a</u>	Department of Pathology SA	April 1992	Alan Shore?	
<u>12b</u>	Update: Does Infection Cause Coronary Disease?	Nov. 1997	P. Welsby	P15
<u>13</u>	International Journal of Medicine		Garth Nicholson	
<u>14</u>	Res. Vet. Scient.: Lympho. Subpopulations in Peripheral Blood of Sheep Experimentally infected with Tick-Borne Disease	July 1991	Woldehiwet	
<u>15</u>	Journal of Clinical Immunology (US): Lymphocytes Phenotype and Function in the C.F.S.	Jan. 1993 13 (1)	Strauss et al.	P30
<u>16</u>	S. Maryland Clin Immunol.	Jan 93 13 (1)		P30-40
<u>17</u>	Affidavit: "To Whom It May Concern" to the SA Medical Council	January 1995	Dr P. Tarbleton,	
<u>18</u>	Bulletin Académie Nationale de Médécine 1979	N°6 Masson Ed. Paris	Paul Giroud	P163
<u>19</u>	Maladies Infectieuses	1976 Ch 41	J. Orfila	
<u>20</u>	Arch. Inst. Pasteur Tunis: Les Infections Superposées Sont à la Base des Faillites de L'Humanité	1986 Vol 63	P. Giroud J.B. Jadin	P 97-99
<u>21</u>	Study Annales Internat. Med.: CFS: May 12: F. Nightingale's Birthday Comprehensive Approach	1994 - 121	T. Hennessy	P953-959
<u>22</u>	Lancet	Vol 347, April 1996		P977,978
<u>23</u>	Bulletin Academie Nationale Medicine	Vol 163 No 6 1979		
<u>24</u>	Bulletin Societé Pathologie Exotique	January 1952		
<u>25</u>	Lyme Disease CDC			
<u>26</u>	Rickettsiae and Rickettsial Dseases	1973	Brezinia	
<u>27</u>	Bulletin Societé Pathologie Exotique	1969	JB Jadin	
<u>28</u>	Annales of Internal Medicine	January 1995		
<u>29</u>	ASBMT	Vol 3 1952	JB Jadin	
<u>30</u>	EEG report of 18 year old Epilectic	February 1998	CL Jadin	
<u>31</u>	An Emerging Group of Pathogens in Fish	1997 Oregon S U Synopsis	JL Fryer M. Mauel	
<u>32</u>	SAMJ Tetracycline in ME - fad or fact?	Vol 82 1992	Bettina Schön	
<u>33</u>	Pharmalogical Basis of Therapeutics	1991	Goodman et al	

The Rickettsial Approach
Dr. CL Jadin

<u>34</u>	In vitro susceptibilities of Rickettsiae	1997	University of NC	
<u>35</u>	Relation entre Protozoaires, Virus et Bacteries	1984	JB Jadin	
<u>36</u>	Arthropods			
<u>37</u>	Martindale	6 th Ed 1995		P314-318
<u>38</u>	Rickettsial Disease - Review of Medical Biology	Ch 21 1980	Jawetz	
<u>39</u>	8 th Congress of American Rickettsioses Society	1990	M. Drancourt. P Levy	
<u>40</u>	Académie Royale des Science d'Outre-Mer	1991	JB Jadin	