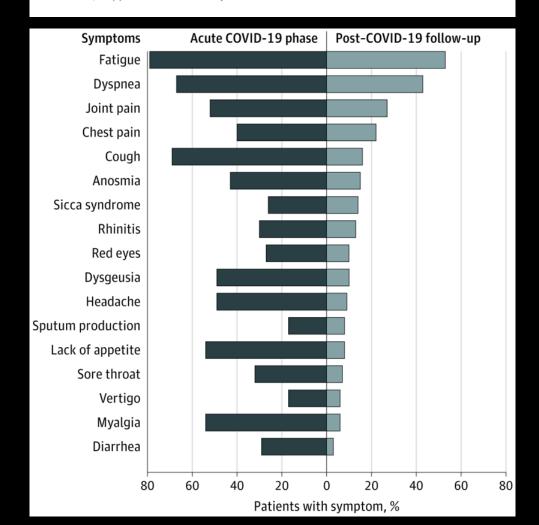
Research Letter

July 9, 2020

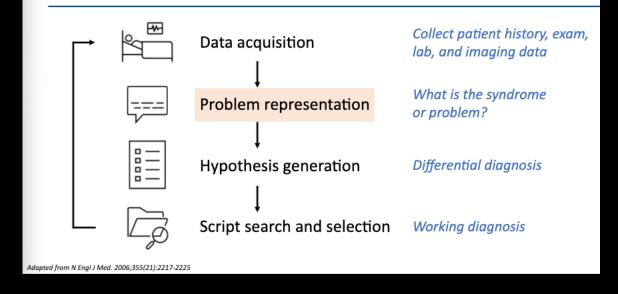
Persistent Symptoms in Patients After Acute COVID-19

Angelo Carfi, MD¹; Roberto Bernabei, MD¹; Francesco Landi, MD, PhD¹; et al

JAMA. 2020;324(6):603-605. doi:10.1001/jama.2020.12603



The Cognitive Steps in Diagnosis



Thinking Slow:

What doesn't fit?

What else could it be?

Could there be multiple diagnoses?



3 months later there was little improvement.

"I am so weak that if I read or write for half an hour I become so tired and faint that I have to lie down,"



Post-Treatment Infectious Diseases Follow-Up

Complete Recovery

Persistent Symptoms: Objective Tissue Damage

Persistent Symptoms:

New Diagnosis

Persistent Post-Infectious Symptoms without Objective Tissue Damage



Irving E. Salit

Post-Infectious Fatigue

SUMMARY

Post-infectious fatigue or post-infectious neuromyasthenia (PIN) is an illness characterized by persisting fatigue and disability after apparent acute infections. In most cases the illness is attributed to a chronic Epstein-Barr virus infection. Symptoms include weakness and fatigue in the absence of physical findings or significant laboratory abnormalities. These patients are frequently depressed and have considerable disability resulting in prolonged loss of time from work. The illness may be persistent or can be relapsing, but often lingers for two years or more. There is no effective therapy. PIN is probably caused by an acute infection occurring in patients who are psychologically susceptible. They require emotional support, reassurance and explanation. (Can Fam Physician 1987; 33:1217-1219.)

Research



Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study

Ian Hickie, Tracey Davenport, Denis Wakefield, Ute Vollmer-Conna, Barbara Cameron, Suzanne D Vernon, William C Reeves, Andrew Llovd, for the Dubbo Infection Outcomes Study Group

Abstract

Objective To delineate the risk factors, symptom patterns, and longitudinal course of prolonged illnesses after a variety of acute infections.

Design Prospective cohort study following patients from the time of acute infection with Epstein-Barr virus (glandular fever), Coxiella burnetii (Q fever), or Ross River virus (epidemic nobarthriis)

Setting The region surrounding the township of Dubbo in rural Australia, encompassing a 200 km geographical radius and 104 400 residents.

Participants 253 patients enrolled and followed at regular intervals over 12 months by self report, structured interview, and clinical assessment.

Outcome measures Detailed medical, psychiatric, and laboratory evaluations at six months to apply diagnostic criteria for chronic fatigue syndrome. Premorbid and intercurrent illness characteristics recorded to define risk factors for chronic fatigue syndrome. Self reported illness phenotypes compared between infective groups.

Results Prolonged illness characterised by disabling fatigue, musculoskeletal pain, neurocognitive difficulties, and mood disturbance was evident in 29 (12%) of 253 participants at six months, of whom 28 (11%) met the diagnostic criteria for chronic fatigue syndrome. This post-infective fatigue syndrome phenotype was stereotyped and occurred at a similar incidence after each infection. The syndrome was predicted largely by the severity of the acute illness rather than by demographic, psychological, or microbiological factors.

Conclusions A relatively uniform post-infective fatigue syndrome persists in a significant minority of patients for six months or more after clinical infection with several different viral and non-viral micro-organisms. Post-infective fatigue syndrome is a valid illness model for investigating one pathophysiological pathway to chronic fatigue syndrome.

have been linked to a diverse spectrum of infections, including brucellosis (which is caused by an intracellular bacterium).7 glan dular fever (caused by the herpesvirus Epstein-Barr virus),* Lyme disease (caused by infection with the tickborne spirochaete Bor relia burgdorferi).9 O fever (caused by the intracellular rickettsia-like pathogen Coxiella burnetii), ii Ross River virus (a mosquito-horne arbovirus found in countries around the Pacific rim), i and viral meningitis (most commonly caused by enteroviral infection).12 By contrast, a comprehensive prospective study of clinical outcomes after other common, more minor, viral infections found no association with prolonged fatigue. Population based prospective studies of the spectrum of post-infective fatigue states are therefore needed to delineate the symptoms and longitudinal course of the post-infective fatigue syndrome; to identify demographic, microbial, immunological, and psychological risk factors; and to determine whether disparate pathogens can precipitate chronic fatigue syndrome.

Methods

Study site

The ongoing Dubbo infection outcomes study is centred on the township of Dubbo in a rural region of southwestern Australia, encompassing a 200 km radius and 104 400 residents (Australian Bureau of Statistics, 2001). The population includes approximately 8% Aboriginal Australians.

articipants

The 94 family practitioners and all four diagnostic pathology albabratories that serve the region cooperated to provide us with habaratories that serve the region cooperated to provide us with record coded reports of all 1gM positive servological results indicating acute Epstein-Barr vianu, Q fever, or Ross River vivan infections. Patients aged 16 years or over, who provided written informed consent, were enrolled through their family doctor. We excluded patients who had symptoms present for more than six weeks or reported pre-exciting medical disorders or drug use likely to be

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Post-infectious fatigue syndrome in dengue infection

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Abstrac

Background: Although the acute manifestations of dengue are well known, few studies have assessed the long-term consequences of dengue infection. We prospectively studied the incidence and factors associated with fatigue in a cohort of patients following dengue infection. Methods: We included patients with serologically confirmed dengue infection admitted to the National University Hospital, Singapore, during a dengue outbreak from October-November 2005. The severity of dengue was graded as dengue fever, dengue haemorrhagic fever and dengue shock syndrome. A follow-up telephone intertive was performed two months following hospital discharge, where a Fatigue Questionnaire was administered. The presence of significant fatigue was considered as the main outcome measure. Significance was assessed at P < 0.05. Results: One hundred twenty-seven patients, 71 (55.9%) males and 56 (44.1%) Females, of mean age 36.06 yeas; (no.1-70.S.D., 13.722), participated in this study. Twenty-five (19.7%) patients had dengue haemorrhagic fever and the remaining 102 (80.3%) had dengue fever. In multivariate analysis, increased age, female seet, the presence of chills, and the absence of rankse were significant associated with the development of fatigue post-dengue infection. There was no significant association between fatigue and dengue severity.

Conclusions: This observation represents the first systematic evidence that dengue can result in clinical disease beyond the acute phases of infection. Host factors, such as age and sex may be important in the puthogenesis of this clinical entity.

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Keywords: Dengue; Fatigue; Risk factors; Pathogenesis

O I Med 2002; 95:527-538

Chronic fatigue following infection by *Coxiella burnetii* (Q fever): ten-year follow-up of the 1989 UK outbreak cohort

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Received 16 October 2001 and in revised form 1 May 2002

Summary

Background: Some patients exposed to Q fever (Coxiella burnetii infection) may develop chronic fatigue.

Aim: To determine whether subjects involved in the West Midlands Q fever outbreak of 1989 had increased fatigue, compared to non-exposed controls, 10 years after exposure.

Design: Matched cohort study comparing cases to age-, sex- and smoking-history-matched controls not exposed to Q fever.

Methods: A postal questionnaire was sent to subjects at home, followed by further assessment in hospital, including a physical examination and blood tests.

Results: Of 108 Q-exposed subjects, 70 (64.8%) had fatigue, 37 idiopathic chronic fatigue (ICF) (34.3%), vs. 29/80 (36.3%) and 12 (15.0%), respectively, in controls. In 77 matched pairs, fatigue was commoner in Q-exposed subjects than in controls: 50 (64.9%) vs. 27 (35.1%), p<0.0001.

ICF was found in 25 (32.5%) of C_0 -exposed patients and 11(14.3%) of controls (p=0.01). There were 36 (46.8%) GHQ cases in C_0 -exposed subjects, vs. 18 (23.4%) controls (p=0.004). A matched analysis of those more intensively studied showed fatigue in 48 (66.7%) C_0 -exposed patients and 25 (34.7%) controls, (p<0.0001), ICF in 25 (34.7%) C_0 -exposed and 10 (13.9%) controls (p=0.004), and chronic fatigue syndrome (CFS) in 14 (19.4%) C_0 -exposed patients and three (4.2%) C_0 -exposed patients were GHQ cases compared to 17 (23.6%) controls (c_0 =0.003).

Ďiscussion: Subjects who were exposed to Coxiella in 1989 had more fatigue than did controls, and some fulfilled the criteria for CFS. Whether this is due to ongoing antigen persistence or to the psychological effects of prolonged medical follow-up is uncertain.

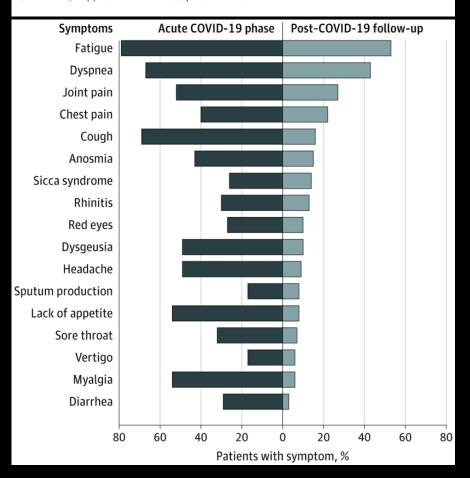
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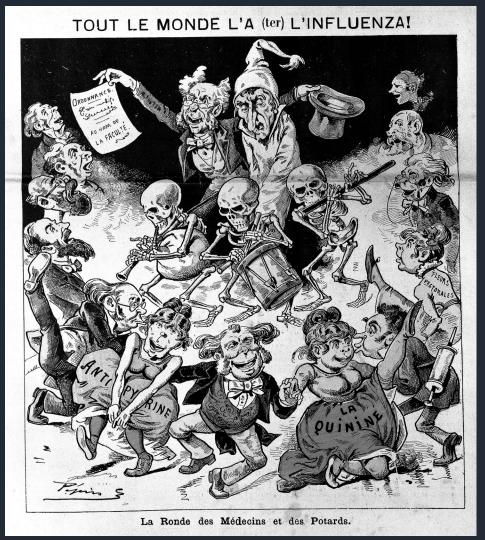
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"I am so weak that if I read or write for half an hour I become so tired and faint that I have to lie down,"

Josephine Butler; following the "Russian Flu" 1890's

