RESEARCH INTO ME/CFS, 1988-1998 – Too much PHILOSPHY and too little BASIC SCIENCE!

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1. WHAT IS RESEARCH?

It is simply an attempt to discover the truth. However, even in 1999, this search may still concentrate on one of 2 alternate pathways:
a) The METAPHYSICAL (or philosophical) route which seeks to establish truth purely by reason and argument.

b) The PHYSICAL (or scientific) path which sets out to determine facts by systematic investigation of material events and by experiment.
The metaphysical approach bears much the same relationship to the scientific as ASTROLOGY (which involves the influence of the stars on human affairs) does to ASTROPHYSICS (which determines the chemical and physical composition of astral bodies).

2. HOW SHOULD RESEARCH INTO ME/CFS BE CARRIED OUT?

a) The first essential is an epidemiological study of HOW MANY are affected in a set period of time

b) Followed by a collection of facts about WHO suffered from WHAT, WHERE and WHEN

c) This data, if carefully documented, should lead to a bright idea about HOW (a) and (b) might be connected (a HYPOTHESIS) which is usually simple and which can be tested by EXPERIMENT or by checking the hypothesis against more newly collected facts .

3. THE HISTORY OF RESEARCH INTO ME/CFS

Three distinct historical sequences have emerged:
a) LATE 19th AND EARLY 20th CENTURIES – The METAPHYSICAL APPROACH
Although ME/CFS may be as old as the human race, there was little scope for the scientific as opposed to the metaphysical approach at this period. Yet, if old medical records are to be believed, sporadic cases of this chronic disabling disease were clearly recognised in civilian and military populations. At that time, civilian cases were said to suffer from NEURASTHENIA (an outmoded umbrella term for a neurosis with symptoms as varied as mental irritability and writer's cramp!). However, in military life, especially following World War 1, the most popular diagnoses were "Shell shock", "Effort syndrome" or simply "Lack of moral fibre" (for which the sufferer could be shot!). As the creator of Sherlock Holmes once remarked, "It is a capital mistake to theorise before you have all the evidence – it biases the judgment"(1.).

b) 1910-1988 – the SCIENTIFIC APPROACH. This was an uniquely productive and exciting period of factual research, at the end of which almost all the data essential for constructing and testing hypotheses about the cause of ME/CFS (which, alone, can lead to

DIAGNOSIS, CORRECT MANAGEMENT and PREVENTION of the disease) was available to research workers.

(i) The sanitary revolution. The mid 20th century had set the scene for phenomenal changes in socioeconomic conditions, public health, medical and technological knowledge when chance, as always in research, favoured the prepared mind. From the 1880's, vast sections of the population of the more affluent countries in Northern America, Canada and Europe moved from crowded urban conditions to sparsely populated well housed suburbs thus, interrupting the circulation of age-old naturally immunising childhood infections. In diseases such as poliomyelitis (formerly a rare, sporadic disease of early childhood) non immune adolescents and adults bore the brunt of the massive epidemics of paralytic polio which followed (paradoxically) in the more affluent communities of the world .

(ii) Observational Medicine. Clinical excellence in those days relied more upon listening, observation, examination and in-depth knowledge of the family history than upon technology. By 1910 it had been noted that epidemics of paralytic poliomyelitis were frequently followed (seasonally and geographically) by an atypical or non paralytic form. This term was originally used to describe these epidemics of ME/CFS, which were noted to differ clinically from polio in that the disease was generally milder but more chronic and liable to relapse. Further observations (eg. in Iceland)(2.) indicated that outbreaks of the one disease could terminate or block the spread of the other. Epidemiology and the regular publication of reliable infectious disease statistics were an acknowledged governmental responsibility. Possibly the best epidemiological review of ME/CFS ever written was by ACHESON in 1959(3.) in which he studied some 15 epidemics and suggested that all might be caused by related agents capable of slightly different clinical activity from place to place or time to time.

(iii) Definition. The term "Myalgic encephalomyelitis" (ME) was henceforth used in the UK, Canada and Australasia to define an illness which, following a virus infection, leads to multisystem involvement of cardiac and skeletal muscle, liver, lymphoid and endocrine organs but which is primarily due to central nervous system dysfunction and subsequent breakdown in bodily homoeostasis. Confirmation of this hypothesis was supported by electrical tests of muscle and of brain function (including the subsequent development of PET and SPECT scans) and by biochemical and hormonal assays. Sophisticated tests of cognitive function (psychometric tests) were also developed. They demonstrated a clear difference between this illness and psychiatric conditions. Notwithstanding, McEVEDY and BEARD(4.), after examining the case histories (but not the patients) 15 years after 292 members of the Royal Free Hospital Staff were involved in a major epidemic of ME, declared the condition to be a manifestation of MASS HYSTERIA (a term inherited from Greek mythology to describe symptoms which may take any imaginable form and are considered to arise from a wandering womb!)

(iv) Virology finally emerged from the dark ages of technical difficulty in which viral infection could be guessed at but seldom proved. From 1948, when tissue culture permitted some viruses to be grown, electron-microscopy enabled others to be seen and the techniques of molecular biology permitted virtually all microbes to be studied (by the amplification and identification of their genetic fragments, even if hidden in internal body organs) the sequence of events in related diseases such as poliomyelitis and ME became clear. During an outbreak of polio and ME in the 1950s, isolation of a whole range of polio and non polio enteroviruses from clinical and asymptomatic patients, indicated that there were some 69 related viruses in

this group associated with a wide range of common acute and chronic infections of children and adults including paralytic poliomyelitis (mainly but not exclusively caused by polioviruses) and with acute viral meningitis, encephalitis, myocarditis, Epidemic Bornholm Disease and Hand Foot and Mouth Disease, infections of the middle ear, skin and eye, to say nothing of chronic myocarditis Juvenile onset diabetes, Myalgic encephalomyelitis and other chronic neurological and motor neurone conditions, caused by a wide range of non polio enteroviruses (Coxsackie, ECHO and enterviruses 68-71)(5). Echo 9 virus was actually isolated from patients during an outbreak of ME in Lancashire during the 1955-56 epidemic years(6.). The rediscovery of the Post-Polio Syndrome (first described in 1870) but brought to the attention of doctors in the USA by patient sufferers one hundred years later, indicated that the polio viruses could persist silently for some 25-40 years after the initial infection. Such persistence has been described in chronic myocarditis and in the internal organs of patients with ME following death by suicide(7.). In the early 1980's,

OLDSTONE(8.) studied viral persistence in 12 additional virus species, in which the infecting virus could alter host cell function without subsequent cell destruction by the immune system. ARCHARD(9.) and colleagues described a possible mechanism for the persistence of Coxsackie B virus in the skeletal and cardiac muscle of sufferers from ME and other diseases in the late 1980s. The production of a specific vaccine for chronic myocarditis is now possible.

c) 1988-1998 – A RETURN TO DISBELIEF?

(i) A new definition for ME. Following successful immunisation against poliomyelitis in the early 1960s and the removal of 3 strains of polio virus from general circulation in the countries concerned, the related non polio entero viruses rapidly filled the vacancy. By 1961, the prevalence of diseases (such as viral meningitis) caused by these agents soared to new heights. In the mid 1980's, the incidence of ME had increased by some seven times in Canada and the UK, while in the USA a major outbreak at Lake Tahoe (wrongly ascribed at first to a herpes virus) led to calls for a new name and new definition for the disease, more descriptive of herpes infection. This definition based on "fatigue"(10.) (a symptom common to hundreds of diseases and to normal life, but not a distinguishing feature of myalgic encephalomyelitis) was designed to facilitate research funded by the manufacturers of new anti-herpes drugs. However, a "fatigue" definition (which also omits any reference to children) has proved disastrous for research in the current decade. Whether in its original form or in the 4 redefinitions which have followed, most research workers, led by the Americans are now calling for an urgent change (omitting "fatigue") so that like can be compared with like in international ME research.

(ii) The metaphysical approach ousts science once again. Although research funding for the study of ME is minimal in the UK, the major sources (totalling some £5 million in recent years) are non governmental agencies such as the Pharmaceutical and other industries. The major beneficiaries are, without doubt, members of the psychiatric profession who have exhumed ancient terms such as "hysteria" and invented new ones such as "somatisation" to explain that patients suffering from ME perpetuate their own illness. Previously reputable medical journals concur with this strange philosophy(11.) and with therapies which compound psychological manipulation and increasing exercise to effect a short term cure. A leading proponent of this approach (who, like Voltaire's Dr Panglos(12.), was discovered teaching his philosophy to young servant maids behind the bushes), has ensured that the very words of a recent leading article on this subject are now inscribed upon a wide variety of

benefit agency, insurance, retirement, and other official forms, which doctors must sign on behalf of their patients. Compared with this bludgeoning of public opinion, the "mass hysteria" allegation at the Royal Free Hospital seems little more than the mad buzzing of a demented fly, and, in 1999, sufferers from ME continue to experience increasing, anxiety, stress and financial hardship.

3. WHAT IS THE PRESENT STATE OF RESEARCH INTO ME?

(i) Only one government (the American) is making a substantial financial contribution to ME research – albeit with some doubt about the proper appropriation and direction of the funds. At the same time, the Americans have proved to be unaccountably timid about epidemiological surveys (the essential basis of research) and investigations into the problems of childhood and adolescence.

(ii) An American symposium on the state of the art. Owing to severe problems in obtaining any adequate funding and in securing subsequent publication for ME research, outside the psychiatric remit, in the UK today, most basic scientific work is performed with difficulty and published abroad. In this manner the US, rather than Britain, now leads world opinion and we have to search the American medical and lay press for up to date information on the state of play:

a) The "Fatigue" definitions still in use, outrageously distort the true prevalence of the illness by up to 100 times (13.). However it is now accepted that occupations exposed to infection (eg. nurses) have an exceptionally high rate of ME compared with the general population. Though similar accounts from the UK, including the effect of infection on the clustering of cases in schools, are freely published there,(14,15.) the initiative to repeat such research is lacking in the USA.

b) Since 1988, the majority of research projects have been restricted to the elucidation of symptoms already recognised in the 1950s. Many scientists now try to persuade us that these symptoms represent the cause rather than the result of a multi -system disease. However, the most useful work relates to brain dysfunction (now confirmed and further explored by the use of brain imaging, eg. Tirelli et al,(16.) and by using physiological methods to compare ME and the Post-polio syndrome, by BRUNO and colleagues(17.)). Cardiovascular, muscle and neurological problems affecting the hypothalamus and autonomic nervous system have all been intensively studied, adding to the evidence that ME is indeed an organic rather than a "psychological" disorder. However, it is sad to note that the section on therapy is almost entirely directed to the psychological approach together with progressive exercise. The opinion that modern immunological research does not confirm ME as a disease of immune dysfunction and that it does not have an unique immunological profile, is reinforced both in the USA and the UK

4. WHAT CAN BE DONE IN THE FUTURE?

As we approach the Millennium, it has to be acknowledged that the struggle for recognition of ME as a serious disabling organic disease with significant requirements for medical social, educational, and financial support has (due to media manipulation of public opinion) entered the realm of politics rather than the more desirable one of basic science. With only a tiny minority of the medical, scientific, legal and other potentially supporting professions on their side, it is the sufferers from ME (especially those who are youthful and have most to lose)

who must make their voices heard in the present debate.
Decisions about the proper funding and direction of research, indeed about whether such work will damage a scientist's career prospects, can only be taken if the present climate of public opinion is challenged. The needs of all sufferers now have to be re-stated loudly and clearly. They include:-

1. Immediate Government funding of a nationwide epidemiological survey in order to establish the true prevalence of ME in the community (including those severely affected who are not under medical supervision). This exercise cannot be funded by small charity efforts and should not be passed over to industrial sponsors. In the absence of such official information, patients with ME cannot assert their rights to adequate medical, social, financial or educational support as for any similar disabling illness

2. Redirection of research to the cause of the illness, for without this knowledge guidelines on the diagnosis, management and prevention of the illness will be unintelligeable and financially wasteful.

3. Redirection of research efforts to schools, health care and other institutions, where there is a high prevalence of ME and clustering of cases, in order to determine the nature of the commonly circulating infections which are able to trigger the onset or relapse of ME. This may prove the most economical and speedy method of determining a means of diagnosis, management and prevention.

4. The assurance that any new definitions of ME will include diagnostic guidelines for children and that research is planned to test cognitive defects and discover educational methods which can prevent a life-long educational deficit in this important age group. The truth is out there and will be disclosed eventually, but much depends on our individual efforts to ensure that we live to see it!

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