AIDS and CFS/ME: a tale of two syndromes*

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ABSTRACT – Both HIV/AIDS and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) presented major challenges for medicine, science and society. This article explores what could have impeded investigation of – and specifically pharmaceutical engagement with – CFS/ME, in contrast to the impressive achievements seen in HIV/AIDS. It explores the obstruction of mind-body dualism in a historical context, and examines some of the possible obstacles to pharmaceutical enquiry. Nothing of real substance is identified that would justify the lack of investment and interest in solutions for patients with CFS/ME.

KEY WORDS: AIDS, chronic fatigue syndrome, Descartes, HIV, ME, mind-body dualism, pharmaceuticals, physicians, psychiatrists

> *It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of light, it was the season of darkness, it was the spring of hope, it was the winter of despair, we had everything before us, we had nothing before us.*
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> (Charles Dickens, *A tale of two cities*)[1]

There are many resonances between CFS/ME and AIDS/HIV. Both are chronic, heterogeneous, life-changing illnesses, in which the many resultant uncertainties and fears are compounded by social stigma, blame and neglect (some of the least endearing of human qualities, and ones from which the profession is not immune). The resulting despair and anger have led people affected in many directions, not always fruitful: turning to unproven therapies of many sorts, displacing their anger on those who are trying to (or are supposed to) help them, and engaging in various forms of activism, targets various.

Both conditions are now very common, though one is epidemic and the other largely endemic. Both have shown strongly the need for a balance between the art and the science of medicine, and for continuity of care. I have set out elsewhere the 'mountain guide' model of the physician, where the traveller-patient is guided through the unfamiliar terrain of illness by someone who knows these mountains well and the possible routes through them.[2] The guide can offer the traveller the different options – scenic, rugged, etc – but whichever way the traveller chooses, the guide will go with them. In both conditions, we have learnt vital lessons from listening carefully to the patients, to what – directly and implicitly – they are saying.

Treatment and treatments

Both conditions have also illustrated the hazards of an over-specified and narrowly interpreted view of 'evidence-based medicine' (did we ever practise anything else?), especially when there has been a need for intervention to support the patient before all the necessary knowledge has been acquired. Thus, as two of us commented in the early stages of the AIDS pandemic: 'The immediate needs of our [current] patients must be met within the limits of what is realistically achievable, without mortgaging the future by sacrificing science for expediency'.[3]

In both conditions, the initial approach has been to apply clinical tools (pharmacological and supportive) developed for other conditions and from other experiences, in both cases with not inconsiderable benefits, although they needed some adjustment and adaptation to the new setting. In both cases, clinicians – conventional and unorthodox – have tried a variety of remedies from their armamentaria, with enthusiasm and varying degrees of scientific rigour and detachment.

But thereafter the contemporary medical history of these conditions seems to diverge. Whereas the prospects for people with AIDS and HIV have been completely transformed over some 15 years of pharmaceutical medicine and its products, those of their companions with CFS/ME remain little changed.

Although the pathways through the wilderness of drug development and treatment trials for HIV infection have not been easy or even straight, the pace has been incredible and unprecedented. With HIV/AIDS, we were fortunate to have the necessary tools in immunology and virology, as well as the conceptual framework we needed. Jonas Salk asked in 1989: 'What might have been our fate if … HIV

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had occurred before [we had] the armamentarium to deal with it?!'[4] Perhaps the answer is that we would be in the sort of place where CFS/ME now is!

Causation and treatment

Interestingly, the early part of the AIDS epidemic seemed to start out in a not dissimilar way to CFS/ME. There were many speculations about aetiology and pathogenesis.[5] These included: allo-immunization by sperm, antigen overload, poppers, strange worms, Aleutian disease of mink, African Swine Fever Virus, cytomegalovirus, human T-cell leukaemia virus type 1 (HTLV-I) (though the published paper was changed) and lymphadenopathy-associated virus (LAV), identified by Montagnier's group in Paris, later called HTLV-III and, later still, HIV. The discovery of HIV and the resulting therapeutic focus, embodied by AZT (azidothymidine, zidovudine) as the first antiretroviral agent to be used clinically, were in some ways the beginning of a different paradigm.

Thus, the late Roy Porter, the incredibly productive medical historian, commented:

> *Medicine may express confidence about the 'medical model'; within that model, however, enormous scope remains for disagreement and controversy. This is nowhere better seen in our own time than with the question of AIDS… Early in the epidemic speculation was rife that it might be the consequence of disastrously injurious lifestyles… Once again, medical hypotheses and moral judgements had seemingly become confused. There was therefore great relief when a viral source (HIV) was identified in 1984.*[6]

Similarly, Virginia Berridge, in her fascinating and authentic contemporary history, *AIDS in the UK*, notes:

> *Biomedicine was defining the chronic disease model. The role of AZT… was crucial in defining the image of AIDS as a set of biomedical problems, open to chemical resolution.*[7]

So perhaps for AIDS the defining moments were the identification of its aetiological agent, and a means of suppressing it.

Yet certainly with AZT, science combined the rationalist approach with good fortune (said to favour the prepared mind):

> *AZT was one of many compounds which had been on pharmaceutical companies' shelves for many years… It had been taken down off the shelf and tried experimentally, as part of the desperate search for anything which might be of some use in the treatment of AIDS.*[7]

The use of antiretroviral agents themselves has provided further evidence of the central role on HIV in AIDS, and has given new insights into pathogenesis.

Biomedical and biopsychosocial approaches

Biomedical solutions are insufficient in themselves, whether for AIDS/HIV, or any other condition. What they can do is provide some anchorage against shifting social constructs of illness, of which perhaps CFS/ME is one of the most evident current exemplars.

Key Points

HIV/AIDS and CFS/ME provide illuminating challenges to science, medicine and society, and they have both similarities and contrasts

Mind-body dualism creates a serious obstacle to contemporary analysis of problems such as CFS/ME, although the paradigm had some utility in enabling earlier scientific progress

Pharmaceutical interest and investigation of CFS/ME has been modest, but potential obstacles are similar to those that were successfully overcome for HIV/AIDS

However, biopsychosocial or holistic perspectives, sensitive to the needs of the individual and aware of the complexity of society, are also essential, if we are to be effective in guiding our patients through the unfamiliar terrain of illness, whatever biomedicine has to offer or not. The 'Both/And' construct!

As the late historian, Roy Porter, comments:

> *Medicine has largely embraced the model of the physical sciences, a materialist reductionism – which is by no means self-evidently right for comprehending the true character of all kinds of human sickness. For, as the graveyard of discarded 'diseases' shows, medicine has often stuffed into disease envelopes strange collections of clinical symptoms, social phenomena, and prejudices.*[6]

Thus, in my view, biomedical approaches (the 'science') must be combined with – not seen in opposition to, as some would have us believe – biopsychosocial ones (the 'art') for the complete physician, who 'heals sometimes, relieves often and comforts always'.

I wish particularly to explore some of the possible reasons why CFS/ME has yet to attract the interest, enthusiasm, energy, sense of emergency, and – above all – the resources of pharmaceutical medicine, and its corporate embodiments. After all, the early apothecaries would certainly have been dispensing to people with CFS/ME, whatever they called it at the time. They would have been keenly aware of its huge social and personal impact, not to mention the market opportunities!

Before I do so, however, I need to explore some crucial background ideas about illness and in particular about the mind-body dualism, most explicitly expressed by Descartes. This is evidently a crucial context for comprehending some of the present disputes/misunderstandings about CFS/ME.

Mind or body; body and mind

It is puzzling indeed to me to see how the concept of a separateness of mind and body can have continuing legitimacy in contemporary medicine and science. Whether as a neuroanatomist manqué, or as a physician, this distinction seems to me to be such an absurdity: The anatomical, let alone the physiological, substrate for the mind provides all the complexity that one could possibly need for brain and mind, without detracting from the

concept and the mystery of mind. And all my patients have minds and bodies, which are fully connected and interacting!

So perhaps we should explore the historical context of this dualism, which now also permeates social attitudes, and understand it, before we escape from the imprisonment of our own conceptual history!

At least in Western philosophy, science and medicine, according to Bertrand Russell:

> *Descartes brought to near completion, the dualism of mind and matter, which began with Plato and was developed, largely for religious reasons, by Christian philosophy…The Cartesian system presents two parallel but independent worlds, that of mind and that of matter, each of which can be studied without reference to the other…*
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> *There is in Descartes an unresolved dualism between what he learnt from contemporary science and the scholasticism that he had been taught. This led him to inconsistencies, but it also made him more rich in fruitful ideas than any completely logical philosopher could have been.*[8]

While I have lately been inclined to bemoan the consequences of Cartesian dualism, Roy Porter sets out a compelling case for Descartes as someone, who by this means enabled and catalysed modern scientific development, with Galileo, liberating it from religious constraint:

> *Descartes postulated two radically different entities, extension (material) and mind (immaterial). Only the human soul or mind possessed consciousness. 'Extension' … was a legitimate terrain for scientific investigation. By Descartes' deft manoeuvre, mind had, so to speak, been mystified, while body was laid bare. Such a demarcation clearly had attractions for medicine. If the body's working were purely 'mechanical', its territory must be the exclusive property of medical science. A huge KEEP OUT notice had, as it were, been pinned to the body, excluding theologians, moralists, and anyone else considered fishing in medicine's pond … The mechanical world-view with its attendant mind-body dualism unleashed an extraordinarily productive programme of anatomical and physiological research.*[6]

Physicians and psychiatrists

Moreover, in a quite fascinating essay, Pressman elaborates the complex and changing interactions between mind and body, the physician and the psychiatrist.[9] Tellingly, he heads it with a quote from Shakespeare's *King Lear*: 'We are not ourselves when nature, being oppressed, commands the mind to suffer with the body' – arguably true of any illness! He says:

> *Descartes' philosophical tour de force of dualism, although known for splitting the analysis of the mind from the analysis of the body, nonetheless spurred research into the somatic mechanisms that commute a volition into an action…*
>
> *As the physiological and bacteriological terrain came into sharper focus, so too did those areas in which medicine was admittedly ignorant. Paradoxically, as our scientific knowledge becomes increasingly sure, leading to even higher expectations, those problems that cannot be solved, develop an increased capacity to threaten our faith in science…*
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> *Psychiatry's peculiar domain is precisely those problems that baffle regular medicine. It is psychiatry's intra-professional obligation to deal with these problems, shoring up the faith that, although no precise medical answers yet exist, they are still medical problems. Ironically psychiatry is despised by the rest of medicine [and by society at large] for this lowly but vital role …*
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> *That a given disease, once understood, is no longer considered psychiatric is thus not so much a loss for psychiatry as it is an indication of what has been psychiatry's true function… Once a disorder is well understood, psychiatry's proper business with it has in fact come to an end.*[9]

I mention this, in part because of its compelling wisdom, happily distant from the gross prejudices about psychiatry and psychiatric disorder that seem so prevalent (but probably always were), but also because it allows me to acknowledge the important work done by colleagues in psychiatry in the management and exploration of cognitive, behavioural and physiological interventions in CFS/ME.

Possible obstacles to pharmaceutical interest in CFS/ME

In going on to explore the need for (and possible reasons for the lack of) pharmacological interventions for this condition, I do not diminish the importance of the parallel work on these other approaches. Indeed, cognitive behavioural therapy remains a crucial part of our therapeutic response for problems faced by people with HIV, much as rehabilitative techniques are relevant to patients recovering from intercurrent diseases in AIDS. Once more, 'Both/And' applies. But our patients need more.

And where are pharmaceutical medicine and the pharmaceutical industry? Why are they not buzzing around this honey pot in the way they did with HIV/AIDS? The list of pharmaceutical agents studied to date,[11] mostly with negative results, is a sad litany of varied ideas of mixed provenance.

Let us explore some of the possible obstacles to more substantial investigation of CFS/ME from a pharmaceutical medicine perspective, and consider their validity.

1 The problem of the name(s)?

> *Nor bring, to see me cease to live,*
> *Some doctor full of praise and fame,*
> *To shake his sapient head and give*
> *The ill he cannot cure a name.*
>
> (Matthew Arnold, *A wish*)

Sometimes called the disease of a thousand names, none is satisfactory.[11] (Similarly, it is said that, if there are a thousand treatments for a condition, there are none.) 'Chronic fatigue syndrome' is a wholly inadequate vehicle to convey the experience, while 'myalgic encephalomyelitis' (or 'encephalopathy') implies a manifestation that is not always present, and a pathogenic mechanism and locus that are not established. An eponym would be ideal. But AIDS and HIV had other names before, and the definition of AIDS changed over time, so this cannot be a

sufficient reason not to proceed. Ongoing disputes about the name are, however, a serious distraction.

Not helpful, but not necessary.

2 Little known of its aetiology and pathogenesis?

There are numerous examples in the history of medicine and of pharmaceuticals where a treatment has emerged serendipitously or through careful observations in advance of knowledge of disease causation or mechanisms. Obviously, if such knowledge is available, it does help to bring focus, as seen with HIV/AIDS.

Not necessary, but would be helpful.

3 Dissent among professionals?

There is nothing new here, though the natural disputatiousness of professionals is certainly heightened in a relatively data-free zone. Opinion is used to fill the vast gaps in knowledge and hypothesis tends to be more emotionally appealing (or the reverse) than the dry, but ultimately supreme, data. Yet legitimate disagreement can even fuel the engine of investigative science, as was seen in AIDS.

Not helpful, but maybe inevitable.

4 Patient activism?

AIDS and CFS/ME have seen both the good and the bad face of activism, the former directed at disease and social disease, the latter directed at individuals and organisations.[12] The best of it – and the majority of it – can ensure more and more effective and informed research and care. The worst of it, such as personal attacks and the thoughtless demonisation of industry, are both destructive and inhibiting to further involvement. As with AIDS, we should expect to focus on the positive, and see the negative side of the coin as a sadly necessary concomitant that can be contained.

Not unhelpful, and maybe necessary.

5 Fringe versus mainstream?

Marginalisation of patients and of conditions is an inevitable consequence of the current lack of knowledge and understanding. The stigma reflects the fear and threat of the unknown and of what we find hard to comprehend or manage personally or professionally. Nonetheless, it can provide a ready excuse for ignoring difficult problems. In AIDS, this phase was mercifully brief. In CFS/ME, it seems slow to end.

The involvement of fringe, complementary or alternative medicine and practitioners in conditions which are difficult to treat, is entirely unsurprising, reflecting unfulfilled need. Their holistic approach, and the time they may offer, can be a great benefit for patients. However, some of the therapies espoused are poorly secured scientifically, and can be a distraction or even a deterrent to scientific engagement. In HIV/AIDS, the emergence of treatments with demonstrable efficacy restored a better balance.

Not surprising, but not always helpful.

6 Potential agents are unfashionable and imprecise?

When one looks at the sort of agents that have been used for CFS/ME, they are a strange mix, deriving from a range of different domains of medical practice, and constructs of the condition. This is again a reflection of the lack of firm data, but they can provide some serendipitous clues. It was much the same in the early years of AIDS. Some types of intervention for CFS/ME may show enough promise to justify further exploration, while others can already be put to one side.

Inevitable, but not necessarily unhelpful.

7 Size of the market?

The epidemiology is increasingly showing ME to be a common problem,[11] with a recent community-based study giving a prevalence of about 0.4%.[13] This is well beyond the projected size of HIV/AIDS in the industrialised world when pharmaceutical interest and investment began.

Not a problem!

8 'Evidence'?

We must ensure that the lack of a formal and high-level 'evidence' base is not used as an excuse for not developing one. As with other emerging problems, including AIDS, we will have to start by picking up early clues, most of which will come from the careful analysis of patient and clinician experience and observation.

First get your evidence!

9 Heterogeneity and chronicity?

There is some disagreement about whether CFS/ME is one condition or several, or whether there are definable subgroups that may differ in aetiology, manifestations, severity, natural history and prognosis, or response to treatment. As with any condition (eg HIV/AIDS, diabetes mellitus), studies must ensure that interventions are investigated in a way that can take account of the observed variability, however it is explained or defined. It is inescapable that the patients with CFS/ME who need treatment are those whose condition is chronic with a low trajectory, complicated by changes resulting from other variables. It was not so difficult to identify ways of dealing with such a timeframe and complexity in HIV/AIDS.

Inevitable, but they mean long and large or focused studies.

10 Lack of clear outcome measures?

The review of pharmaceuticals studied to date[11] noted the lack of agreed and validated outcome measures that would be essential for study design. This needs to be resolved urgently, but it is not unusual. The role of different clinical outcomes and surrogate markers posed major challenges in trial design for many years in HIV/AIDS. While new studies can be used to identify and validate such measures for CFS/ME, we should, as in other conditions, take existing tools that have been validated

in comparable conditions or settings, together with those that show promise in previous studies.

Not for the first time, but needs sorting.

Aims and objectives

It is strange that this article should finish with a heading more usually found at the beginning. There are some simple things that we can start our investigations with, such as a systematic investigation of existing symptomatic measures as applied to CFS/ME. This is analogous to early trials of treatment for opportunist diseases in AIDS. With a range of disabling symptoms such as muscle pain, nerve pain, sleep disturbance, gastrointestinal disturbance, vertigo and impaired cognitive function, there is no shortage of choices for the application of existing agents.

The main challenge, however, is to investigate something directed at the underlying cause or process, whatever these may be.

There seems to be no sound basis for the lack of investment of ideas and resources in CFS/ME. The agent, or agents, that could help these patients recover from their devastating illness may already be on the shelves, like AZT, which was the 'beginning of our exploration' of truly effective therapies for HIV and AIDS. The challenge for us and the patients together is to find out.

Centuries after the first accounts of what we now call CFS/ME, do we have the will to do it? What are we waiting for?

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