8. We need to find reliable bio-markers for ME (more)

Charlie Starwyne was asked by his friend Nora (our zookeeper from section 1) to take a look at her flightless birds. Charlie was excited to take on the project, because he had a special interest in the flightless Dodo bird, and he considered all modern flightless birds to be direct descendants of the Dodo.

Charlie set about to study the features of the birds and see if he could determine why they didn't fly. He checked to see whether their heads were disproportionately large. He examined all the tails and compiled average statistics, but still didn't see anything interesting. Charlie could find no reason at all why these birds wouldn't be flying.

This is, of course, another silly story. But it is the counterpart to how CFS is often being studied today. Rather than identify what makes ME/CFS different to other diseases (including symptoms like post-exertional malaise), many researchers have just grouped together a very mixed group of patients who do not have a specific diagnosis, simply because they share a common general symptom: fatigue.

Biomarkers, treatments, and other particular features of a disease cannot be found by approaching the problem in this manner. Any biomarkers or other specifics are drowned out by all the other conditions in the selection group. There are two logical ways to approach the problem of the heterogeneous (mixed/unlike) set. One is to subgroup. It is likely that the Oxford criteria would still be unsuitable, because there is nothing in its requirements to unify the characteristics of the patients. The second approach is to define the research criteria more particularly in an attempt to collect a less heterogeneous sample. While there are good reasons to think that, with a bit more care, many patients who are currently being labelled with 'CFS' would be more appropriately diagnosed with an already-established diagnosis, it is possible we might need to create another disease title and definition (or more) for those who do not meet the very tight criteria but cannot yet be diagnosed under any existing disease category.

It is possible that, much as emus, ostriches, cassowaries, kiwis and rheas are closely related, ME/CFS may be a spectrum of related diseases. Some other researchers have used the Fukuda criteria for ME/CFS, (which is an improvement, although not a tight as the proposed I.C.C. definition, which we recommend for research purposes), and have made some interesting findings.

Here are just three of them – all very important markers of something seriously wrong.

1. There is markedly reduced function of NK cells (a type of immune cell which should function in defence against germs). This finding is well-replicated, dating at least from 1987.

2. There is typically reduced blood flow in the brain, which worsens after exercise.

3. Consistently, researchers have found evidence of oxidative stress, which Taha et al. describe as a "*central mechanism in various pathological conditions.*"

It is difficult, if not impossible, to obtain biomarkers from a mixed sample of fatigued patients, unless that sample is so large that we can identify sub-types. There rarely is funding for such large studies: motivation and skill are not enough.

An efficient solution, as recommended by a recent new definition, the “International Consensus Criteria", would be to adopt tighter sets of criteria for future research, which would include patients who are severely ill and who are currently omitted from the majority of studies.