

FEATURE

CHRISTMAS 2011: ORAL TRADITIONS

Cod liver oil and tuberculosis

Malcolm Green revisits an 1848 study of cod liver oil in the treatment of tuberculosis

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The Royal Brompton Hospital is well known for studies evaluating the use of streptomycin and other chemotherapy for tuberculosis (TB) in the 1940s to 1960s, but it is less widely known that the physicians at the hospital were already investigating treatments for TB 100 years earlier. This is a report of a study conducted in 1848.

- Objective: to investigate the use of cod liver oil in the treatment of consumption (also known as phthisis, and now called tuberculosis or TB) in 19th century London
- Hypothesis: that cod liver oil might arrest progression or reduce the death rate from consumption
- Protocol: the study was conducted in 1848 at the Hospital for Consumption and Diseases of the Chest, Brompton (fig 1). The results were presented to the hospital's Committee of Management in the *First Medical Report of the Hospital for Consumption and Diseases of the Chest* in 1849.¹

In their report, the medical officers *felt it their duty to bear testimony to the judgement evinced in the selection of the site for the hospital: The hospital is built on a dry gravelly soil, in a suburb of the metropolis long celebrated for its salubrity, sheltered on the north and east by the metropolis and open to the south and west; the wards are lofty and the corridors light and capacious.*

542 inpatients with consumption were treated with cod liver oil, in a dose of 1 drachm (3.6 ml) three times a day, gradually increased, in some few cases up to 1.5 ozs (42 ml) per dose. The oil is straw coloured, transparent and free from offensive smell. Patients take it in general without repugnance. It is usually administered in camphor-water, aromatic water, bitter infusions, milk or any other agreeable fluid. When there is great irritability of the stomach it has been given in mucilage of gum with a few drops of hydrocyanic acid.

The patients treated with cod liver oil were compared with 535 patients who received standard treatment alone (without cod liver oil). Patients were *classed according to the amount of benefit they received*. The term *improved* includes patients in whom the symptoms are *relieved* or *much relieved*. The term *arrested* means that *all or nearly all of the symptoms have disappeared, the patients feel well and are able to pursue their ordinary occupations. The other terms speak for themselves.*

Results

There was no important difference in the number of patients who *improved* in the two groups (standard treatment 61% v cod liver oil 63%; table 1). However, in 18% of patients given cod liver oil, the disease was *arrested* and when it is *recollected that of the whole number otherwise treated the disease was arrested in only 5%* the value of this remedy must be considered *very great*. Furthermore, 33% of patients given standard treatment alone deteriorated or died, compared with only 19% of those given cod liver oil.

It was observed that *one of the most striking effects of the use of cod liver oil is an increase in the patient's weight. A gain in weight occurred in 70%, a loss in only 21% and in 9% the weight remained stationary*. However, the weight changes in patients in the control group were not recorded, so this observation remains anecdotal.

Discussion

The authors state in their report, *No other conclusion can be drawn than that cod liver oil possesses the property of controlling pulmonary consumption to a greater extent than any other agent hitherto tried*. The results seem to support this conclusion. Tuberculosis was arrested in 18% of the patients given cod liver oil, compared with 6% of those in the control group. Deterioration or death was reduced from 33% to 19%. For patients with consumption, these results represented a massive improvement in prognosis and must have been greeted with enthusiasm by doctors and patients alike.

The study, however, had several weaknesses:

- This report is not a new study and has been previously published, so fails the test for original work. However, the implications of the 1848 study for generations of children and adults over the succeeding 160 years merits recording it a place in the modern literature. The *First Medical Report of the Hospital for Consumption* is not widely available (indeed only one copy is known to exist) and is not referenced in PubMed or Google
- There is no bacteriological confirmation of the diagnosis, since *Mycobacterium tuberculosis* was only recognised and described by Koch in 1892, some 43 years later

- No radiographic confirmation was available until Roentgen's discovery of x rays in 1895
- No statistical analysis was done, not least because Fisher only introduced coherent statistical methods in 1922. There is no record of how patients were allocated to the two groups
- Ethical permission, patient consent, structured randomisation, and double blinding had not been invented. There were no local, regional, or national ethics committees to consider the protocol
- The present author (MG) cannot vouch for the collection of the original data or for its veracity. However, the recordings made in the report are convincing.

On the other hand, the study had a number of strengths:

- Studies on other treatments (inhalations, other animal and vegetable oils, naphtha) were reported as negative, although further details were not given
- The number of patients in the two groups probably gives the study sufficient statistical power
- The end points seem to be carefully recorded, particularly death.

The use of cod liver oil in the treatment of tuberculosis was widely practised in the late 19th and early 20th centuries. Cod liver oil was advertised and marketed across the world (fig 2). Children were given cod liver oil, presumably as a preventive measure (fig 3). This practice continues to the present day. In a random survey of doctors who entered Oxford University medical school in 1960, all 35 doctors recalled being given cod liver oil as children, but did not know why. A similar survey of medical students at Imperial College London in 2005 showed that just under 30% (10/32) had been given cod liver oil, but again did not know why.

Death rates from tuberculosis in the United Kingdom and the United States declined steadily throughout the 19th and 20th centuries (fig 4).² This has been attributed generally to better living conditions: reduction in overcrowded living might have reduced transmission. Probably more important was improved nutrition. It could well be that the widespread use of cod liver oil encouraged by doctors played a significant part.

Vitamin D

Along with tuberculosis, rickets was a common and debilitating condition in children in the 19th and early 20th centuries. Studies of diet in animal models of rickets showed the beneficial effect of cod liver oil, and its antirachitic factor was identified in 1922 by McCollum and colleagues, who named it vitamin D.³ A role of sunlight in preventing rickets had long been suspected and, in 1923, photosynthesis of vitamin D in the skin was described.⁴

Vitamin D is now known to be involved in activating macrophages to inhibit multiplication of mycobacteria and to induce peptides which destroy mycobacteria.^{5 6} Indeed, vitamin D deficiency could lead to an acquired immunodeficiency and an impaired host defence reaction to mycobacteria.⁷ Patients presenting with tuberculosis tend to have lower levels of vitamin D than matched controls⁸ and in one study, 76% were vitamin D deficient.⁹ It is reasonable to conclude that a lack of vitamin D increases susceptibility to tuberculosis, and can contribute to clinical deterioration of the disease.

A role for vitamin D in combating tuberculosis gives a rational basis for sunshine therapy, which was widely practised for patients in sanatoriums before chemotherapy became available.

Patients were put out on their beds to lie in the sun in summer and winter, and many were sent to Switzerland and other sunny countries for treatment.

A role for vitamin D in immune defence against tuberculosis might explain other curious findings. Immigrants from the Indian subcontinent have a higher incidence of active tuberculosis in the UK than in their own country.¹⁰ They also have generally low levels of vitamin D, attributed to their diet and to the UK's relative lack of strong sunlight needed to synthesise vitamin D in darker skins.¹¹ Hindus have more tuberculosis than Muslims, perhaps because their vegetarian diet contains minimal liver oil or other sources of vitamin D (fish, meat, and dairy products).¹² The effect of vitamin D in stimulating macrophages could explain why non-respiratory tuberculosis was common both in the 19th century and now in immigrants; without effective macrophage function, mycobacteria could spread more easily from the lungs via the blood to other organs.⁶

Conclusions

The 1848 study is an early example of a two arm investigation addressing an important clinical problem. James Lind's famous treatise showing that citrus fruits can treat scurvy¹³ preceded this study by 100 years, but relatively few therapeutic studies were reported in the intervening years. The physicians at the Hospital for Consumption and Diseases of the Chest used rational methodology in 1848 to establish the value of an important therapy, decades before any reasonable explanation for the use of cod liver oil was established. The results might have contributed to the widespread use of cod liver oil as a nutritional supplement, thus playing a part in the remarkable reduction in incidence of and deaths from tuberculosis. Their study must stand tall in the proud heritage of UK clinical investigation.

Tuberculosis is still a virulent and common infection, accounting today for some 3.5 million deaths worldwide.² The emergence of multidrug resistant bacilli is of increasing concern.¹⁴ It could be that vitamin D supplements will again have a role in combating this terrible killer, possibly in some subsets of those patients with vitamin D deficiency through diet or relative lack of sunshine.¹⁵

Competing interests: The author has completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf and declares: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. Provenance and peer review: Not commissioned; externally peer reviewed.

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Table

Table 1 | Results as shown in 1848 study

	Standard treatment	Standard treatment plus cod liver oil
Number of patients	542	535
Improved	60.8%	63.1%
Arrested	5.6%	18.1%
Deteriorated or died	33.3%	18.8%

Figures



Fig 1 Hospital for Consumption and Diseases of the Chest, Brompton

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Dr. J. A. SAUNDERS, Professor of Orthopedic Surgery in Bellevue Hospital Medical College, New York, says: "Of late years it has become almost impossible to get any Cod-Liver Oil that patients can digest, owing to the objectionable mode of procuring and preparing the liver."
Dr. J. SAUNDERS then says: "For some years I had given up the use of Cod-Liver Oil altogether; but since my attention was called to Möller's Oil, I have prescribed it almost daily, and have every reason to be perfectly satisfied with it."
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[Image: Fox Photos/Getty Images]



Fig 3 Good for your chest, too

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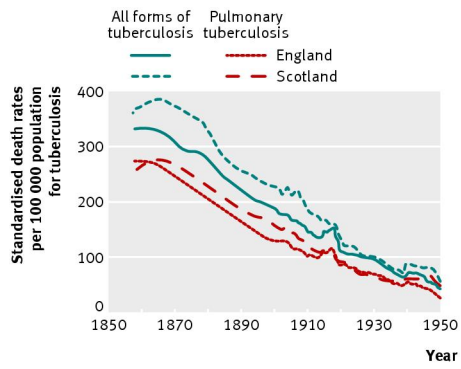


Fig 4 Mortality from tuberculosis, 1860-1950