# Medical History

# History of the treatment of rheumatoid arthritis

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The treatment of an untreatable condition such as rheumatoid arthritis calls forth, as they might well say in Tipperary, great therapeutic skill and expertise. Anybody can cure a curable disease if he happens to have the right drug at hand, but the treatment of a condition for which there is no positive cure makes much greater demands on the doctor, who has to be practical pharmacologist, human being, psychiatrist, and father confessor—he has, in fact, to be a proper physician in the fullest sense of the word.

When no certain cure exists, quack remedies tend to proliferate and the history of quackery and secret cures is full of extraordinary forms of treatment for the various arthritic disorders. Not only the quack cures of the past but also many forms of treatment given with the best will and intentions in the world by the best and most orthodox doctors of the time seem strange to us today. Rheumatoid sufferers have such pain and discomfort every day of their lives that they live eternally in high hopes of something effective turning up. For this reason they are optimistic and open to persuasion, for any form of treatment, however odd and apparently stupid, may well work initially. In 1951, when many people, both patients and doctors, thought that the newly discovered cortisone of Philip Hench was the therapeutic answer to this disease but were for one reason or another unable to obtain it, a paper from Sweden stated that similar results could be obtained by injections of deoxycortone (Doca) and ascorbic acid. Such was the expectant electric atmosphere of the time that our outpatient clinic acquired a Lourdes-like quality. Patients who had not fully extended shoulders or elbows for many months dramatically did so, walked corridors briskly, and, in one case, jumped over the bed. The second injections had less impact, however, and the third failed to do any good whatsoever. A year later I asked one of these patients what treatment had ever done her any good? "None whatsoever!" "What about the double injections we gave you a year ago?" "They were no good at all!" "But this is what you wrote at the time and this is your own handwriting of a year ago: 'I haven't felt like this for years. It's a miracle. I have no pain and can move easily and freely.' What about that?" And looking rather hurt and baffled all she could say was "I must have been crazy at the time I wrote that." Crazy or not it worked while the enthusiastic heat was on, but what we got to know as the triple response to faith healing was the rule: excellent, fair, nil to first, second, and third treatments respectively. Only a few patients can maintain that continuous complete faith in the future that transcends pain and depression.

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## "Cures" for arthritis

For some two years I was chairman of the research subcommittee of the Empire Rheumatism Council, now the Arthritis and Rheumatism Council. Many so-called cures for different forms of arthritis were sent to us, though the type of arthritis treated was seldom defined. They fell into three main groups: group 1 (the therapeutic group): if you take X (or Y or Z) you will recover from arthritis; group 2 (the prophylactic or never group): if you take Y (or X or Z) you will never get arthritis; group 3 (the never-never group): if you never take Z (or X or Y) you will never get arthritis.

This last group was the smallest. Five principal poisonous substances were incriminated as aetiological agents. If these were always avoided the afflicted would remain free from arthritic symptoms. They turned out to be simple substances, present in every home, their sombre potentialities being hidden under a simple exterior: salt, tap water, milk, tea, and marmalade. Certain gases, noxious fumes, eyestrain, and certain postures and stances were also incriminated, but less often. Group 2, the never or prophylactic group, was also small compared with group 1. Iodine lockets, string shirts, underwear made of special material such as flannel (particularly red), sheep wool, angora wool, clothes made of modern synthetic fibres, and so on, would ward off arthritis. Pendants round the neck, bangles round the wrists or ankles, potatoes or nutmegs in the pocket are as old or older than civilisation, carrying the same prophylactic magic as any juju in an African witchdoctor's armamentarium. These are the age-old lucky charms, protecting the wearer by their own particular magic, and the most popular today are copper bangles, which are worn not only by intelligent human beings, but also sometimes by their racehorses, dogs, or cats. A cord round the waist will prevent arthritis in the spine today just as it prevented the evil eye, ague, or the creeping palsy in mediaeval times. A Scottish patient combined both preventive agents cheaply and effectively by suspending a copper coin on a gut string tied round the waist; for the modest price of 1d he thus secured freedom from arthritis of both peripheral joints and spine.

The first or therapeutic group was the largest, and it was encouraging to note that out of about 200 cures only 16 were secret remedies, the details of which could be revealed only at a price or on full and proper compensation. External applications of different sorts were common, as were fluids and salts of different sorts and combinations to be taken by mouth, special herbs, diets, and baths. Certain rays, emanations, and radioactive substances were quoted, as were different types of mud; and, in sharp contrast to group 3, there were several advocates of simple tap water to be taken in large amounts every day, though others found rainwater preferable and more effective. It is quite clear from the existence of these cures that the age of magic and faith is not yet over. *Homo sapiens* is still *Homo credens*.

## Diet

The influence of diet on body processes is a very real one, and "natural"—that is, understandable—explanations are preferred by most patients and indeed by their doctors also. Fasting is one of the oldest forms of treatment for rheumatoid arthritis and one that does occasionally seem to produce improvement, but all too often the rheumatoid patient is already thin, anaemic, debilitated, and if anything mal- or even under-nourished. All sorts of diets have been advocated in the treatment of rheumatoid arthritis, but rarely is any

improvement seen, and there is no evidence that the disorder is nutritional in origin. Vitamin C deficiency is present in a few cases but is as likely to be the result of food faddery and over-stringent diets as of the opposite. The anaemia of rheumatoid arthritis is very much part of the disorder in most cases, worsening or improving roughly in parallel with the activity of the rheumatoid disease, but dietetic deficiencies do play a part in some cases.

## Infective agents

Infective agents also crop up with cyclical regularity. Undoubtedly certain infective agents, such as the rubella virus, can cause an acute arthropathy of rheumatoid type, but the disorder settles rapidly and does not become chronic. Possibly, as with rheumatic fever, a known infective agent triggers off a chain of events that produces the full disease picture, but so far this has not been shown in human tissues often and regularly enough to convince most workers. This has not, however, stopped many empirical antibacterial and other anti-infective treatments being tried, from the sulpha drugs onwards. It is of interest that gold salts were first introduced into medicine because they were thought to be effective in the treatment of tuberculous disease. Because rheumatoid arthritis was an inflammatory disorder possibly of the same (tuberculous) origin, gold was tried in this disease on an anti-infective basis and found to be helpful. An effective treatment was therefore once again introduced on a false theoretical basis.

## Some past treatments for rheumatoid arthritis

Much has been said of the barbarity of blood letting and leeching in the old days, but we still have acupuncture today, and, more rarely, moxibustion, cupping, and various other forms of physical treatment that are comforting and reassuring but little more. It was only 30 years or so ago that we had Speransky's pump, a few millilitres of cerebrospinal fluid being removed from the theca by lumbar puncture, then reintroduced, then aspirated again, the procedure being repeated several times. Given a few patients who benefit with any form of treatment (and some invariably do) and no sensible rationale at the time, one will soon be invented. What is protein shock or cytotoxic treatment in one decade may become immunosuppressive treatment in another, and the beneficial effects of one and the same form of treatment may be explained in terms of endocrine imbalance, alarm reaction, or autoimmune reaction in successive decades. Old forms of treatment also breed new forms: if one heavy metal improves the patient, why not try another? Gold is still orthodox and effective treatment, but bismuth, arsenic, and copper injections are no longer given. Clinical improvement after antibacterial treatment in rheumatoid arthritis usually means either that the diagnosis was wrong or that bacterial infection coexists with the rheumatoid disease. It is fair to say that almost any drug that has done any good in any other disorder has been tried in the treatment of rheumatoid arthritis, and if faith and optimism are present in either patient or doctor some good results will be obtained for a time in every case, the highest proportion occurring when abundant faith is present in both doctor and patient, particularly if the latter has complete faith in the former.

The late Dr Philip Hench used to show an alphabet of cures in rheumatoid arthritis. The following is my own version.

**A**cupuncture; apple diet; auto-haemotherapy; angora wool
**B**ee venom; bangles, copper; Baths, various
**C**hemotherapy; copper salts; crows' meat; cobalt
**D**oca and ascorbic acid; diet
**E**xtractions of teeth and other septic foci; ECT
**F**asting; fever; faith; fango
**G**in; guaiacum; gelatine; green-lipped mussel
**H**eat; honey; hope; hypnotism; hayseed
**I**nsulin injections; iodine; inner cleanliness
**J**aundice, induction of
**K** vitamin; kaolin compresses
**L**ourdes; love
**M**ud; magnetism; moxibustion; mistletoe
**N**utmeg; nettles
**O**live and other oils, oral and intra-articular
**P**lacenta extracts; prayer; procaine; polyvinyl clothing
**Q**uinine substitutes
**R**hubarb; rest
**S**peransky's pump; sulphur; spa therapy; seaweed
**T**ransfusions of blood, fresh or pregnant; tiger balm
**U**ltrasonics; underwear, anti-rheumatic; urea
**V**itamins; vertebral manipulations; vaccines
**W**hale, standing inside; worms, earth-; water
**X**mas snow
**Y**oghurt; yoga
**Z**am-Buk; Zyloric (allopurinol)

All these forms of treatment, however odd, have been or are being used and all have given good results on occasion. In a disease that naturally waxes and wanes any treatment given at the time of an improvement may be given the credit for that improvement. Some of the forms of treatment noted in this alphabet of cures are rare enough to be generally unknown and need, therefore, some explanation. The crows' meat cure comes from Victoria, Australia, where some years ago an elderly Chinaman in Melbourne was paying 50p each for live crows. Apparently fresh crows' meat mixed with spirits is a centuries-old Chinese cure for "rheumatism." The hayseed cure comes from Wales. The earthworm hails from Glasgow, where its originator found that if several large earthworms were put into an airtight tin in a dark place for two weeks they would exude a rancid oil which when rubbed on the affected parts would effect great improvement or cure. From Australia came the whale cure; standing inside the thorax of the dead stranded mammal was said to improve arthritic pains greatly. Eventually the aroma became so strong that the inhabitants of this stretch of coast in New South Wales insisted on the removal of the therapeutic carcase. The Christmas snow cure depends, like the seawater cure, on walking barefoot in it. However odd and bizarre the treatment, at some time benefit has been claimed for it, though at other times (as with more orthodox treatment) there may be no result, worsening, or the advent of undesirable side effects.

### CORTISONE

In the context of this article, the interest of cortisone lies in the therapeutic theories it produced at the time and the new forms of treatment to which these theories gave rise. Hench noted that in pregnant women and in patients developing jaundice the rheumatoid disease often remitted or improved greatly, which led him to search for a naturally occurring substance that could cause such a remission. Arising from these observations, blood from pregnant women was transfused into rheumatoid sufferers, placental extracts were tried, and jaundice was induced artificially to produce remission. It had previously been noted that rheumatoid patients on gold treatment sometimes developed jaundice and that when they did so they often improved greatly. At the time this jaundice was thought to be a toxic effect of chrysotherapy, but in retrospect it seems more likely to have been due to serum hepatitis conveyed by the needle and syringe.

At this time Selye's theories of stress held the stage, and the beneficial effects of spa treatment were considered in 1950 to be possibly due to adrenocortical stimulation and increased glucocorticoid output, rather than to simple physical and psychological factors. Although Hench used cortisone in initial dose of 300 mg/day in what he called a physiological trial rather than a therapeutic one, and though he later rapidly reduced the dose and advocated no more than 35 mg/day in divided doses in the treatment of rheumatoid arthritis, so dramatic were the results at the higher dose and so great were the patients' demands at the time, that the next 10 to 15 years saw all the bad effects of corticosteroid overdosage. These years are already part of the history of therapeutics and applied (and misapplied) pharmacology. High-dose corticosteroid therapy qualifies completely for inclusion in this article. Overdosage still continues in therapeutics in other branches of medicine, but happily is now seen much less often in the treatment of rheumatoid arthritis. Corticosteroids remain highly effective and very useful tools in this disorder at conservative dose levels, whether one believes the basis of the disease to be infective, postinfective, autoimmune, endocrinological, or even psychosomatic in origin.

### ELECTROPLEXY AND INSULIN TREATMENT

The introduction of electric convulsion therapy (ECT) and insulin treatment into psychiatry made a great impact and fundamentally changed current forms and ideas of treatment. A short burst of electricity through the brain was found to produce more benefit than months of psychoanalysis and "talk therapy" in many patients. As dramatic cures were occasionally seen in rheumatoid arthritis after overwhelming near-fatal disease, and as a school of thought favoured the central nervous system as the fons et origo of rheumatoid arthritis, ECT and insulin coma were both tried. Once again some patients improved, and once again most failed to do so. Psychiatric overtones are not uncommon in this disease so that symptomatic improvement might have been expected in some patients, but lasting remission occurred only very rarely. Indeed, major stresses of any kind while occasionally appearing to switch off the disease just as commonly

switch it on! Relapse occurs after major stress even more often than remission.

SPAS, HEALTH RESORTS, AND CLIMATE

The one thing that the British man in the street is convinced of is that cold and damp cause rheumatoid arthritis, along with all other forms of "rheumatism." He is also sure that diet has something to do with it. In the past large establishments have been set up, usually as business enterprises, to cure arthritis by physical means and diet. These establishments are still thriving and new ones are still appearing, and though labels change they are still based essentially on the same therapeutic approach. The ancient and modern spas, the modern cure houses and health centres, still have their appeal, as they had to the ancient Romans and the Ephesians before them; but very often the weak, thin, anaemic, and ill rheumatoid sufferer deteriorates while the more robust, obese, osteoarthrotic patient benefits under such treatment. Warmth, rest, relaxation, and the proper diet for the individual concerned are all good treatment and a warm dry climate suits most (but not all) better than a cold wet one. Sunshine has an excellent morale-raising effect also, particularly in people in northern climes.

Treatment at such health resorts may produce symptomatic improvement, but the word "cure" widely used in this context is a misnomer. The fact that only in the last 60 to 70 years has rheumatoid arthritis been distinguished from a host of other disorders such as gout, osteoarthrosis, and Reiter's disease makes retrospective diagnosis impossible. Whatever the disease was of which great-grandmama was cured at the spa, it was almost certainly not rheumatoid arthritis.

## Yesterday's orthodoxies

As stated previously, only within the last 70 years has rheumatoid arthritis been separated diagnostically from other forms of arthritis and even today diagnostic confusion occurs, particularly between generalised osteoarthrosis and rheumatoid arthritis in women at the menopause, and occasionally between polymyalgia rheumatica (polymyalgia arteritica) and rheumatoid arthritis in older subjects of either sex.

Among three old books on my shelves, Bain and Edgecombe (1905)[1] refer to arthritis deformans (or rheumatoid arthritis) as occurring in four different types: acute or subacute, a more progressive deforming type, a senile form, and the form in which Heberden's nodes are a prominent feature. Clearly only the first two are what we would now call rheumatoid arthritis. These authors exclude Still's disease, which they consider a separate entity caused by infection. For treatment they advise adequate nutrition, treatment of the indigestion, which they consider part of the complaint, spa therapy with a variety of waters to swallow and to bathe in, and physical measures of different kinds. Wilcox, in Price's *Textbook of the Practice of Medicine* (1934),[2] divides rheumatoid arthritis into two types—primary, and secondary to infection. He emphasises that the most important step is to find out the cause ot the infection which gave rise to the arthritis by full radiological and bacteriological investigation of alimentary, respiratory, and urinary tracts, and then to remove the "infective foci." Vaccines are advocated and also iodine and iodides and intestinal antiseptics such as guaiacol carbonate, salol, dimol, or cyllen, together with rest and suitable physical measures and local applications. In Tidy's *Synopsis of Medicine* (1939)[3] we approach what might be called present-day therapeutics for the first time, and it is really only since the second world war that rheumatoid arthritis and its treatment have received the recognition they deserve by the medical profession as a whole.

## Conclusion

Natural remission occurs fairly often in rheumatoid arthritis and this explains why long-continued treatment of any variety may sometimes appear to produce remission. Drugs that do reverse the inflammatory reaction in rheumatoid arthritis, such as the corticosteroids, are rapidly followed by relapse on stopping the drug. In general, whatever happens to be the drug of the moment tends to get the credit for what is often, in fact, an inexplicable natural remission.

With so many false cures abounding, not surprisingly doctors sometimes have an agnostic, highly critical attitude that the patient does not always share. The danger here is that a useful treatment is sometimes not given by the doctor though the patient might have gained real advantage from it. Like thyroid treatment in myxoedema, it may be disbelieved for many years by the medical profession, the untreated patients paying the price of professional incredulity. There is no harm in inducing a placebo response provided that the substance used does not also cause a nocebo—that is, a toxic—response. Indeed, through the ages, this is essentially what, with analgesics, rest, and simple physical measures, the rheumatoid sufferer has been getting in the past, and what in some cases he is still getting today.

## References


1 Bain, W, and Edgecombe, W, *The Physiology and Therapeutics of the Harrogate Waters, Baths and Climate applied to the Treatment of Chronic Disease*. London, Longmans Green, 1905.

2 Wilcox, W H, in *Textbook of the Practice of Medicine*, 4th edn, ed F W Price. London, Oxford University Press, 1934.

3 Tidy, H L, *A Synopsis of Medicine*, 7th edn. Bristol, John Wright, 1939.


*What, if any, are the toxic effects of the common practice of dusting the roots of brassica plants with 4% calomel paste (4% mercurous chloride) and also what are the long-term ecological risks in soil so treated?*

The toxic action of mercurous chloride is because of its reduction to mercury and mercuric chloride in the presence of alkalis. Mercury forms highly undissociated linkages to sulphydryl groups present in all proteins, as well as with other ligands such as amine, phosphoryl, and carboxyl groups, and is, therefore, a potent, though non-specific, inhibitor of many enzymes even at low concentrations. The calomel paste used for controlling brassica club-root should not be hazardous provided that hands and arms are well protected and any skin accidentally contaminated is immediately cleaned. (Mercurous chloride is absorbed directly through the skin, alimentary tract, and lungs, though skin absorption is generally thought to be too poor for acute poisoning to be a problem.) People using calomel without skin protection run the risk of developing mercurialism in the long term, although no cases have been reported. The threshold limit value (TLV) for mercurous chloride is 0·05 mg/m$^3$.[1] As mercurous chloride is strongly phytotoxic, its agricultural uses are limited. The current background level of mercury in fruit, vegetables, eggs, and meat is below 0·05 ppm and when crops are treated in accordance with good agricultural practice the residue should not exceed 0·1 ppm. Use of this particular formulation will certainly have contributed to the total environmental mercury load.[2] It has been estimated that it may take 100 years to clean polluted waters of their present mercury loads.[2]

1 *TLVs—Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1975*. American Conference of Governmental Industrial Hygienists, Cincinnati, 1975.

2 Lofroth, G, *Methylmercury. A review of health hazards and side effects associated with the emission of mercury compounds into natural systems*, Bulletin No 4, 2nd edn. Stockholm, Swedish Natural Science Research Council, 1970.

*What risk is there to the lacrimal sac and ducts and to the eyes in radiotherapy for treating a rodent ulcer on the bridge of the nose? What type and length of treatment are involved?*

Nowadays those specialised units dealing with the treatment of cutaneous tumours near the eyes tend to send most patients to radiotherapy departments for treatment as the complications are usually minor. There is certainly a slight risk of blockage of the lower canaliculus should this be in the field of radiation, but as this would probably have been involved in any surgical treatment this is no contraindication in itself. As "soft" $x$ rays—that is less than 100 Kv—are used with full eye protection (by placing a lead contact shell in the conjunctival sac) there is no risk to the eye, particularly the induction of cataracts. The only slight complications seen in the lid are epilation and the presence of small hard plaques on the conjunctival aspect, which are normally of no importance.