affects the brain, causing delirium, but also other organs, the heart and lung, and may cause fatal syncope or respiratory failure.

Many years ago Dr S. L. Mitchill (1764-1831) pointed out in America the resemblance which exists between symptoms of poisoning by snake venom and infective fevers.@@1 S. Weir Mitchell and others have shown that serpent venom consists chiefly of albumoses, and the toxins formed by infective bacilli have a somewhat similar chemical nature. Calmette and Fraser found that when small doses of snake venom, insufficient to cause death, are injected into an animal, temporary disturbance is produced; but after a few days the animal recovers, and a larger dose is then re­quired to produce any symptoms. By gradually increasing the dose the animal becomes more and more resistant, until at last a dose fifty times as great as that which would at first have produced immediate death can be injected without doing the animal any harm. If a horse be chosen for the experiment, a considerable quantity of blood may be withdrawn without injuring the animal. When this is clotted the serum is found to act as an anti-venin, so that when mixed with the venom of a snake it renders it harmless. Although this result is best obtained when the venom and serum are mixed in a glass before injection, yet if they be injected at the same time in different parts of the body the animal will still be protected and the poison will not produce its usual deadly results. What occurs with snake venom takes place also when the toxins are formed by microbes, and a new method of treatment by anti-toxic serums has been introduced of late years with great success. This is most commonly and successfully used in the treatment of diphtheria. This disease depends upon the presence of a bacillus which grows rapidly at the back of the throat and in the air­passages specially of children, causing the formation of a mem­brane which, by plugging the windpipe, causes suffocation and death. At the same time it produces a poison which causes inflammation of the nerves, leading to paralysis, which some­times proves fatal. By growing this bacillus in broth a toxin is formed which remains in solution and can be separated from the bacilli themselves by filtration. This toxin-containing broth is injected into a horse in increasing doses, just as in the case of the serpent venom, and after the resistance of the horse has been much increased it is bled into sterilized vessels and the blood is allowed to coagulate. The serum is then removed and its anti-toxic power tested by ascertaining the amount necessary to counteract a given amount of active toxin in a guinea-pig of a certain size, the standard weight being three hundred grammes. The serum, the strength of which has thus been ascertained, is distributed in bottles and injected in the proper quantity under the skin of children suffering from diphtheria. If used at an early stage of the disease, and in sufficient quantity, the results are wonderful. The same method of serum therapeutics has been used in other infective diseases, but not with the same success.

Another therapeutic method which is historically much older than that of serum therapeutics is that of inoculation.

The virulence of infective diseases varies in different epidemics, and at different times in the same epidemic. It had been noted that many infective diseases did not attack an individual a second time, the first attack appearing to protect from subsequent ones. The idea of inoculation, therefore, was to infect an individual with a mild form of the disease, so that he should escape infection by a more virulent one. This was tried largely in the case of smallpox, and once at least by Dr Erasmus Darwin in the case of scarlet fever. The worst of this method was that the disease thus inoculated did not always prove of a mild character, and in the case of Dr Erasmus Darwin’s son the scarlet fever was exceedingly severe and very nearly proved fatal. To Edward Jenner we owe the dis­covery that vaccination protects against smallpox, and it is now generally acknowledged that smallpox and vaccine are

probably the same disease, the virus of which is modified and its virulence lessened by passing through the body of the cow. Pasteur found that the germs of anthrax could be cultivated outside the body and their virulence weakened either by growing them at too high a temperature or in an unsuitable medium. By inoculating first with a weak virus and then with others which were stronger and stronger, he was able completely to protect oxen either from the effects of inoculation with the strongest virus or from infection through contact with other animals suffering from the disorder. On the other hand, he found the weakened virus could be again strengthened by inocu­lating a feeble animal such as a guinea-pig a day or two old with it, and then inoculating stronger and stronger animals: an in­crease in strength was gained with each inoculation, until at last the virus could attack the strongest. A similar increase in virulence appears to occur in plague, where animals, especially rats and mice, seem to be affected before human beings, and not only increase the virulence of the microbes, but convey the infection. Two methods of protective inoculation have been used. In one, Haffkine employs the toxins obtained by growing plague bacilli in broth for five or six w,eeks, and then heating the whole to 650 or 700 C. so as to destroy the bacilli. This preparation is prophylactic, but does not seem to be curative. Yersin has prepared a serum from horses in the same way as diphtheria anti-toxin, and this is said to have a curative action during the attack. In the same way sterilized cultures of typhoid bacilli have been used to protect against attacks of typhoid fever, and an anti-typhoid serum has been employed with intent to cure. Protection does seem to be afforded, but the curative action of the serum is still somewhat doubtful. Although the anti-toxins which are used in the cure of infective diseases are not dangerous to life, yet they sometimes cause unpleasant consequences, more especially an urticarial eruption almost exactly like that which follows eating mussels or other shell-fish. Sometimes the swelling of the skin is much more general, so that the whole body may be so swollen and puffy as exactly to resemble that of a person suffering from advanced kidney disease. These disagreeable results, however, are not to be compared with the benefits obtained by the injection of anti-toxic serum, and this method of treatment is likely to maintain its place in therapeutics.

For many years pepsine has been used as a remedy in dys­pepsia to supplement the deficiency of digestive juice in the stomach, and it has been used popularly in dyspepsia for a still longer period. From time immemorial savages have been accustomed to eat the hearts of lions and other wild animals, under the belief that they will thereby obtain courage and strength like that of the animal from which the heart had been taken, but in 1889 Brown- Séquard proposed to use testicular juice as a general tonic and stimulant. Observations were made on the connexion between thyroid gland and myxoedema, which appeared to show that this disease was dependent upon atrophy of the gland. Accord­ingly the liquid extracts of the gland, or the gland substance itself compressed into tablets, have become largely used in the treatment of the disorder. The success which has been achieved has led to the use of many other organs in a raw or compressed form, or as extracts, in other diseases; *e.g. of* suprarenal capsule in Addison’s disease, of bone marrow in pernicious anaemia, of thymus and suprarenal capsule in exophthalmic goitre, of kidney in renal disease, and of pituitary body in acromegaly. To this method of treatment the name of organo- therapeutics or opo-therapy has been given. The first scientific attempt to employ portions of raw organs in the treatment of disease was made by Lauder Brunton in diabetes in 1873, sixteen years before Brown-Séquard’s paper on the effect of testicular juice. From considering the nature of diabetes, he had come to the conclusion that many cases were due to im­perfect oxidation of sugar in the body; that this oxidation was normally carried out by a ferment in the muscles, and that probably the disease was in some cases dependent upon ab­sence of the ferment. He tried to supply this by giving raw

@@@1 Quoted by Weir Mitchell, “ Researches on the Venom of the Rattlesnake, *Smithsonian Contributions* (i860), p. 97.