

DIPHTHERIA VACCINES

ANTI-TOXIN:

Von Behring performed animal experiments into immunity to diphtheria by blood serum therapy. He published a paper in 1890, listing five methods by which animals could be made immune, but admitted "All five methods of immunization against diphtheria thus far described are, in my opinion, not practicable - at least in the form I have given them [to animals] - for humans"(1). It is said that von Behring's anti-toxin was used clinically for the first time on 24 Dec 1891 - but this has never been fully verified; and claims that two colleagues treated a critical case of diphtheria with the anti-toxin are doubted as insufficient serum was available as it was exclusively obtained from guinea pigs and sheep(2). Anti-toxin was in clinical use by the end of the year - but some children treated with von Behring's anti-toxin died anyway(3).

In 1894, Roux announced he had developed an anti-toxin from horses, and that the fatality rate had fallen from 50% to 25% with his treatment(4) - but in 26 out of every 100 babies given the Roux anti-toxin died(5).

TOXIN-ANTITOXIN:

Toxin-antitoxins were produced and tested in animals in the 1900s - and between 1913 and 1924, 14 varieties of toxin-antitoxin were used in (6), where in 1926 a programme was started to eradicate diphtheria(7) - but cases of, and deaths from, diphtheria rose - from 7,530 cases and 477 deaths in 1926 to 10,776 cases and 642 deaths in 1928(8). Two years later, 'Journal of Medical Society of New Jersey' reported "During the period covered by the increased use of toxin-antitoxin, the incidence of serum disease has also increased"(9).

In 1932, Alexander Glennie, who had produced an antitoxin from horses, which was, later, found to immunize guinea pigs(10) - said in 'Lancet':

"It seems evident from these experiments that a toxin-antitoxin mixture which proved harmless when tested on guinea pigs might be poisonous in a child"(11).

TOXOID-ANTI-TOXIN (TAM)

By 1934, TAM was the most commonly used diphtheria prophylactic in Britain(12) and still in regular use(13) - despite a year earlier, Dr Saunders noting in the `Lancet`: "It must not be forgotten that reactions of the utmost severity may occasionally be encountered with toxoid-antitoxin and many cases come under our notice in which the whole of the upper arm has been involved in an intense inflammatory reaction accompanied by marked prostration"(14).

TOXOID-ANTI-TOXIN FOLLICLES (TAF)

To try to surpass reaction to toxoid-antitoxins, TAF was introduced in the 1930s(15), but when in 1936, TAF was administered to children in a TB sanatorium, the third injection exacerbated the tuberculosis(16).

RAMON'S TOXOID (Anatoxine)

Ramon reported, in 1924, that he was able to immunize guinea pigs with his toxoid(17), which became known as Anatoxine(18). Five years later, reports were being received that patients were refusing to complete the course of treatment because of adverse reactions to the toxoid(19). Despite this, a law in France, in 1938, made Ramon's toxoid compulsory(20). French cases of diphtheria rose from 13,569 in 1940 to 46,539 in 1943(21).

ALUM-PRECIPIATED TOXOID (APT)

APT was used in 1932 and its use spread(22). Five years on, reports began to appear of toxoid-induced abscesses in humans(23).

INCIDENCES of DIPHTHERIA and MASS VACCINATION

In some countries cases of the diphtheria increased - in 64,138 cases in 1932 to 149,971 in 1936; in Copenhagen, Denmark from 41 cases in 1942 to 1,754 in 1944(24); in Holland from 1,273 cases in 1939 to 56,603 in 1943(25); in England and Wales there were 46,283 notifications in 1940, the next year (with a mass vaccination program)

there were 50,797 cases(26).

The British Ministry of Health changed the rules for diagnosis of diphtheria - so the figures showed a "reduction" - in 1944 29,949 notifications(27) reduced to 23,199(28); 1945 25,246 notifications(27) reduced to 18,596(28); 1946 18,283 notifications(27) reduced to 11,986(28); 1947 10,464 notifications reduced to 5,596(29); 1948 8,035 notifications reduced to 3,560(29); 1949 4,982 notifications reduced to 1,881(30).

DECLINE of DIPHTHERIA

* In England and Wales , mortality fell from 100 per 100,000 children in 1860(31) to 40 per 100,000 children for the period 1861-70(32) - before the introduction of immunization.

* In Leicester, mortality per 100,000 fell from 17 in 1920, to 4 in 1923; and with practically no vaccination, continued to fall to 2 per 100,000 in 1932(33).

* In Nottingham, mortality per 100,000 fell from 34 in 1920, to 4 in 1923; and with practically no vaccination, continued to fall to 3 per 100,000 in 1932(33).

* In Northampton, mortality per 100,000 fell from 10 in 1920, to 4 in 1923; and with practically no vaccination, continued to fall to 1 per 100,000 in 1932(33). Dr Stephen Rowland, Medical Officer for , wrote in 1933 "Immunisation has not been practiced in this town, the marked decline in diphtheria during recent years having come about without any artificial means..."(34).

* In England and Wales , there were 18,566 cases of diphtheria in 1944, falling to 14,186 in 1945(35). Despite 56% of under 1 year-old children being unvaccinated, and 72% unvaccinated in 1951, cases of diphtheria fell to 155 in 1955, down to 51 cases in 1956(36).

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