TREATMENT OF DIPHTHERIA WITH REFINED ANTITOXIN

BY

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It has long been known that antitoxin is associated with a soluble globulin in the serum of immunized animals; many attempts have been made to concentrate serum and so reduce the volume of each dose—and, incidentally, troublesome serum sickness; for concentration, ammonium sulphate and sodium sulphate have been mostly employed.

From January to August, 1938, 200 diphtheria patients were treated in Belvidere Hospital with Burroughs Wellcome refined antitoxin prepared by Pope's (1938) process. This is antitoxin prepared by a process of enzyme disaggregation followed by differential heating; the antitoxin-containing molecule is much smaller than that in ordinary concentrated serum. The antitoxin was administered without desensitization of the patient, even though fifty of the 200 gave a history of previous injection of serum. No adrenaline was administered, but it was always at hand in case of emergency. Patients with cervical adenitis were given chewing-gum.

Diphtheria bacilli were obtained from 189 of the 200 patients, using McLeod's medium (Anderson *et al.*, 1931) in the first fifty cases, and Kerrin and Gaze's (1937) medium in the others. Sixty-three cultures were of the gravis type, fifty-two intermediate, and seventy-four mitis. Gravis and intermediate yielded a somewhat higher percentage of the more severe attacks than mitis, the five deaths all being due to gravis. Of the sixty-three gravis patients fifty-seven received serum before the fifth day, and forty-one were children under 10, the period in which the mortality rate is highest.

TABLE I

Method of Injection	No. of Patients	Antitoxin Units			Disappearance of Membrane, Discharges, or Glands (in hrs.)		
		Average	Max.	Min.	Average	Max.	Min.
Intramuscular ..	100	25,200	128,000	8,000	44	108	16
Intramuscular and intravenous ..	50	63,300	200,000	16,000	68	120	12
Intravenous ..	50	19,300	48,000	8,000	47	156	8

Reactions

Intramuscular Group (100 Patients).—No appreciable increase of temperature or pulse rate and no serum reactions or rashes occurred.

Intramuscular and Intravenous Group.—A slight reaction, with transient nausea and an increase of pulse rate by 10 beats and 2° F. rise of temperature, passing off in eight hours, occurred in an adult female who had some years previously received scarlet fever antitoxin. No serum rashes developed in this group.

Intravenous Group.—Two males, aged 16 and 18, with no history of previous injection of serum, showed definite immediate reactions. Both received 40,000 units. The elder patient felt faint, giddy, and sick, and had some difficulty in breathing, slight cyanosis, and an increase of 3° F. in temperature and of 30 beats per minute in pulse rate. The other showed a rise of 2° F., and his pulse increased by 20 beats per minute. Both patients were given 0.5 c.cm. of adrenaline hydrochloride intramuscu-

larly, and they immediately recovered. No patient in this group developed a serum rash.

The following table gives some records of serum reactions.

TABLE II

	Serum Rashes	Pyrexia
Rolleston (1929)*	66.4	—
Metropolitan Asylums Board (1928)* ..	30.3	15.7
Metropolitan Asylums Board (1928)† ..	28.4	4.96
Hunt (1932)	28.1	—
Davis (1938)	17.3	—
Present Series	0	1.5

* Whole. † Concentrated serum.

Complications

The figures in Table III indicate a definite reduction in the percentage of complications.

TABLE III

	Serum	Albuminuria	Paresis	Death Rate
Carter (1933) ..	Ordinary concentrated	71.8	33.7	24.8
Tannahill (1936) ..	"	96.5	53.5	9.5
Carter (1936) ..	"	5.0	24.0	8.0
Present series ..	" Refined "	6.5	11.0	2.5

General Notes

There were no reactions when the serum was given by the intramuscular route, and only slight reactions when it was given intravenously. There were five deaths, two occurring in patients who were moribund on admission and who died within a few hours; the other three were due to cardiac paralysis. The percentage of gravis bacilli in this present series (31) is very high compared with that of Carter in this same area (3.1 and 10.5 in different series), and this makes the 2.5 per cent. death rate a strikingly low figure.

Conclusions

Among 200 patients treated with refined diphtheria antitoxin (Pope) the death rate was only 2.5 per cent. No serum rashes were recorded, and immediate reactions after intravenous injection were few. The small bulk of the serum caused less discomfort to the patient than ordinary concentrated serum.

The percentage of gravis diphtheria in the Glasgow area seems to be on the upgrade.

Chewing-gum appears to be useful in adenitis, apparently causing massage of the cervical glands by the action of the jaw in chewing.

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