

Not Official.

THERAPEUTIC AGENTS OF BACTERIAL ORIGIN.

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THERAPEUTIC SERA.

Syn.—ANTI-SERA, OR ANTITOXINS.

These are obtained by treating an animal with subcutaneous or intravenous injections of increasing doses of (1) bacterial toxins, (2) bacterial cultures, living or killed, (3) a combination of 1 and 2, then bleeding the animal, allowing the blood to coagulate, drawing off the serum and bottling this in the fluid state or after drying *in vacuo*; all these operations being carried out under the strictest aseptic precautions. To the fluid serum a small quantity of an antiseptic is usually added, and each bottle or vial generally contains a single dose only. The dried serum should be in the form of thin scales or fine powder, otherwise it is difficult to dissolve; for use each gramme (corresponding to about 10 c.c. of fluid serum) of the solid is dissolved in 5–10 c.c. of cold distilled water, previously sterilised by boiling.

The therapeutic sera in most instances retain their activity for several weeks at least if kept in a cool, dark place—preferably an ice-safe; they should not be administered with any other substance, must not be heated, and a bottle of the fluid having been once opened, any fluid not used at the time should be discarded. The dried products are preferable in hot climates.

The dose of therapeutic sera corresponds usually to 5–20 c.c. of the fluid serum, according to the activity, which is estimated by ascertaining the amount of serum required to neutralise a given amount of toxin. The dose depends on the gravity of the disease and not on the age of the patient.

The therapeutic sera are administered by subcutaneous injection, in the abdomen or between the scapulae, the skin having been previously disinfected with an antiseptic lotion and the syringe by boiling for five minutes. Early treatment is of the utmost importance.

The therapeutic sera are specific, *e.g.* diphtheria antitoxin is of use only in diphtheria; carefully administered they are harmless, but cutaneous eruptions or joint pains may follow.

The Antitoxins may be used as prophylactics, but the immunity produced does not last longer than three weeks.

DIPHTHERIA ANTITOXIN.—The therapeutic value is reckoned in units, 1 unit being that amount of serum which will completely neutralise 10 lethal doses of toxin in a medium-sized guinea-pig. At least 1500 units should be injected for a dose. Washbourn (*Treatment*, '98, i. 533) recommends 2000 to 4000 units every eight or twelve hours for three days. The prophylactic dose is 200–300 units. Several preparations by different makers can be obtained.

TETANUS ANTITOXIN.—The dose is 10–20 c.c. every six or twelve hours, according to the urgency of the symptoms and the duration of the incubation period.

For prophylactic use, 10 c.c. should be injected every fortnight for six weeks.

In veterinary practice, 20–40 c.c. may be injected every twelve to twenty-four hours, but unless the animal be a valuable one the cost of the treatment is prohibitive.

Tetanus Toxin fixes in the central nerve cells, but these cells evidently do not take up their Antitoxin from the blood, therefore it seems doubtful if the Antitoxin, administered hypodermically or intravenously is of much use for immunising the brain cells. Intracerebral injection enables us to treat tetanus in man on a more scientific basis than formerly.

A method given by Roux and Borrel.—*T.G.* '98, 773.

A method given by Semple.—*B.M.J.* '99, i. 10.

STREPTOCOCCUS ANTITOXIN.—The dose is 10–20 c.c. every six, twelve, or twenty-four hours. Some continental authorities regard this amount as much too small, and administer 50–150 c.c. for a dose.

N.B.—Streptococcus Antitoxin rapidly diminishes in strength with age, and should not be kept.

PNEUMOCOCCUS ANTITOXIN.—The dose is 10–20 c.c. every twelve to twenty-four hours (Washbourn, *B.M.J.*, '97, ii. 1849).

Several other antitoxins have been prepared, but they are of doubtful value. Their dose is usually 10–20 c.c. (plague, cholera, typhoid, tubercle, anthrax, yellow fever, cancer, etc.).

COLEY'S FLUID.

A fluid prepared by cultivating the streptococcus of erysipelas and the bacillus prodigiosus in broth, and heating to 58° C. for one hour.

It has been used in the treatment of malignant growths, especially sarcomata. The dose to commence with is $\frac{1}{2}$ –1 minim, administered by injection in the neighbourhood of the tumour. The dose is gradually increased, the guide being the amount of reaction produced.

TUBERCULIN PREPARATIONS.

A.—KOCH'S ORIGINAL TUBERCULIN.—Prepared by boiling, concentrating, and filtering three months' old glycerin broth cultures of the tubercle bacillus.

An amber-coloured, syrupy fluid, with a characteristic odour. Gives the reactions for glycerin and for albumoses.

The maximum initial dose should not exceed 0.001 c.c., and is administered by sub-cutaneous injection. The injection is followed in tubercular subjects by a rise of temperature of 2–5° F., and constitutional disturbance more or less severe. The dose must not be repeated until the reaction produced by the preceding one has completely passed off. The same dose is administered until it is followed by only a slight reaction, a larger amount may then be given, increasing by 0.001 c.c. until 0.005 is reached, then by 0.002 c.c. and so on.—(Watson Cheyne, *Med. Chirurg. Trans.*, 1891).

For diagnostic purposes the initial dose should not exceed 0.005 c.c., which, if no reaction is produced, may be followed by 0.01 c.c. and 0.02 c.c.

(For the diagnosis of tuberculosis in cattle the dose is 0.1 c.c.—0.2 c.c.)

For the commencement of treatment a 1 p.c. solution is a convenient dilution, later on a 10 p.c. solution. The dilutions should be made with a $\frac{1}{2}$ p.c. aqueous solution of carbolic acid, and only so much prepared as can be used in a few days.

B.—KOCH'S NEW TUBERCULINS.—There are three varieties, termed respectively A., O., and R. Tuberculin R. is the only one of therapeutic value. It is prepared by triturating and emulsifying virulent tubercle bacilli with distilled water, and centrifugalising. The fluid contains 10 milligrams of solid matter per cubic centimetre.

The fluid is administered by sub-cutaneous injection after diluting with sterile

20 p.c. glycerin solution. The preliminary doses should correspond to not more than $\frac{1}{1000}$ of a milligram of solid matter, *i.e.* 0.2 c.c. of a dilution of 1:1000. The injections are repeated every other day, and the dose is slowly increased until it contains 20 milligrams of solid matter, *i.e.* 2 c.c. of the undiluted fluid.

REFERENCES.—*L.* '97, ii. 568, 600, 704, 1488; '98, ii. 194; *B.M.J.* '97, ii. 207; '98, i. 357; '98, ii. 77; *B.M.J.E.* '97, ii. 19, 27, 31, 55, 103; '98, i. 47, 55; *T.G.* '97, 850; '98, 400; *Pr.* lix. 399. Oxy Tuberculin.—*L.* '98, i. 179; *B.M.J.E.* '93, ii. 27.

VACCINES.

GLYCERINATED VACCINE LYMPH is prepared by mixing calf lymph with 50 p.c. of glycerin and storing for three months; this destroys all extraneous organisms.

ANTI-CHOLERA VACCINE is prepared from virulent cultures of the cholera spirillum. Dose 1 c.c. (Wright and Bruce, *B.M.J.* '93 i. 227).

ANTI-TYPHOID VACCINE is prepared from virulent cultures of the *bacillus typhosus* (Wright and Semple, *B.M.J.* '93 i. 256).

ANTI-PLAGUE VACCINE is prepared from cultures of the *bacillus pestis* (*B.M.J.* '97 i. 1057 and 1461).

Some of the antitoxins (Diphtheria, Tetanus, and Streptococcus) may be employed as prophylactics, but their protective power is transient (three weeks), whereas the vaccines protect for at least many months.

MALLEIN.

Prepared by boiling and concentrating broth cultures of the glanders bacillus. Employed for the diagnosis of glanders in animals. The requisite dose is injected sub-cutaneously in the neck. In a glandered animal a large swelling forms at the seat of inoculation, any local lesion becomes enlarged, and the temperature rises at least 2.5 F. above the normal. It is of no therapeutic value.

NUCLEINS.

Prepared by digesting yeast cells, thyroid and thymus glands, etc., with Pepsin and dilute Hydrochloric Acid, and purifying the residue by repeated solution and precipitation in dilute alkali and dilute acid respectively.

A greyish powder soluble in dilute alkaline solutions, insoluble in dilute acids. Contains a considerable quantity of Phosphorus in organic combination, and gives the reactions of proteids.

A very powerful germicide and has been used in the treatment of tuberculosis and other wasting diseases.

DE BACKER'S FLUID.

Pure cultures of yeasts stored under pressure in syphon-like vessels provided with hollow needles by means of which the dose is injected.

Has been used in the treatment of tuberculosis and cancer (*B.M.J.* '97, ii. 802).