

in the extended position momentarily and return relatively slowly to the position of flexion. If the position of flexion is assumed without oscillations of the leg, tone is hypernormal. If oscillations are of wide amplitude and continue for a time, the quadriceps muscle is hypertonic. In spastic paraplegia, for example, if the failure of the hamstrings to relax does not prevent a definite extension, the reflex is delayed; the return to the starting position of flexion is slow, and the oscillations are absent. Finally, the leg hangs in a partially extended position, maintained by the tone of the quadriceps muscle (Fig. 1).

Even in locomotor ataxia the leg does not hang perpendicularly, but in slight extension, though not as extended as in the normal leg. After ramisection the leg hangs perpendicularly (Fig. 2) unless there is contracture of the quadriceps muscle. If contracture is present, the leg will take up an extended posture, and the reduction

of tone after operation will then be indicated by the short period of relaxation.

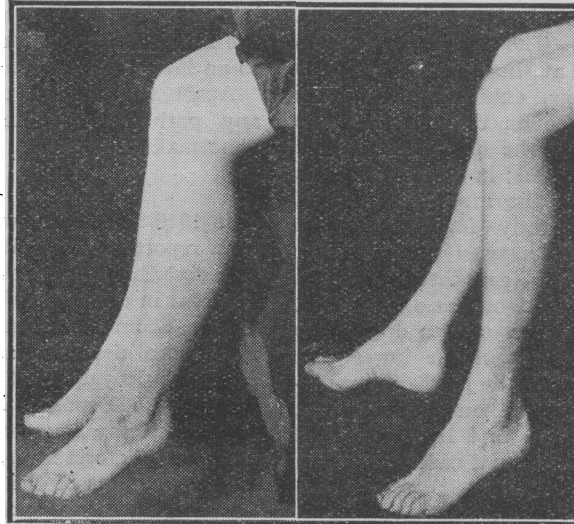


FIG. 1

FIG. 1.—Showing extension of normal leg on stretching the quadriceps muscle.

FIG. 2

FIG. 2.—Showing position of left leg after sympathetic ramisection contrasted with the normal right leg.

#### *Tone as an Indication for Operation*

In Raynaud's disease, Hirschsprung's disease, and Buerger's disease the character of reflex activity, as shown in the knee-jerks, may be used as an indication for operation. In every case of Raynaud's disease and of Hirschsprung's disease that I have personally examined hypertonus has been present. It may be present in Buerger's disease; it is almost invariably present in epilepsy.

In the normal person hypertonia is rarely present. To ascertain this I examined the knee-jerks of fifty medical students. In every instance except three the knee-jerk was normal in relaxation time and in oscillation. Of these three, two students, both mile runners, exhibited hypertonus, and in the other, a victim of

poliomyelitis, the phasic response was absent, and the leg hung perpendicularly from the knee.

## CONVALESCENT SERUM IN PROPHYLAXIS OF MEASLES\*

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Serum or whole blood taken from patients recovering from a disease has often been used in treatment empirically, and with varying results. Thus it has been employed in poliomyelitis, encephalitis lethargica, measles, and scarlet fever.

#### *Historical*

Nicolle and Conseil in 1916 were the first to succeed in protecting with convalescent serum a child who had been exposed to measles. Since then many observers have published their results, and all agree that the value of the serum, if properly used, is very great. Degkwitz in Munich and Debré in Paris control clinics where the serum is collected, prepared, and issued to all who require it, and they have thus treated many thousands of children with very striking results. Debré was the first to point out that the results are even more satisfactory if the serum is used to produce a mild attack rather than complete protection. It is obvious that as soon as a causal organism is definitely established and an animal serum prepared, the human serum will fall into disuse owing to the difficulties inherent in the procuring of sufficient supplies. At present the animal serums available are those of Tunncliff, Degkwitz, and Ferry and Fisher. All these are prepared from a green streptococcus which, it is held though not generally accepted, is the causal agent of the disease. In a comparative

survey of these serums with convalescent serum, Gunn of the Metropolitan Asylums Board showed that:

Ferry and Fisher's serum protected	...	...	0 per cent.
Degkwitz serum protected	...	...	40 "
Tunncliff's serum protected	...	...	43 "
Convalescent human serum protected	...	...	95.7 "

These figures are similar to those obtained by several workers, and show conclusively that, at present, the human serum is by far the most reliable.

#### *Collection and Preparation of Serum*

Since measles occurs mainly in children, it is with the greatest difficulty that we are able to obtain a sufficiency of blood from a donor. We have been fortunate in the co-operation of Dr. Massingham of the London Fever Hospital, where many adult cases of measles are treated, and he has kindly bled these cases for us. Each patient should be carefully examined before bleeding, and the greatest care taken to exclude anyone with the possibility of another infection. Particular notice is taken of any syphilitic or tuberculous taint, and no patient is bled except after a normal uncomplicated measles. Between the seventh and fourteenth days after defervescence 200 to 300 c.cm. of blood is collected aseptically into sterile oxalate solution, this allowing a yield of 50 per cent. of serum after precipitating the oxalate with calcium chloride. Sterility tests and a Wassermann reaction are done on every serum and, if these are satisfactory, 0.5 per cent. phenol is added and the serum is then pooled with several other serums so as to obtain as far as possible a final product of uniform potency. Before use the serum is filtered through a Seitz bacterial filter and a final sterility test done.

#### *Effects of Administration*

No ill effects have ever followed the use of a carefully prepared serum, and any unsatisfactory results can nearly always be traced to insufficient care in the preparation. It is sometimes said that the above technique does not preclude the administration of a tuberculous serum; in

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fact it has been pointed out that since children after measles are particularly susceptible to tuberculous infections, which would not be obvious when they are bled in early convalescence, it must be an unwise and even dangerous practice to bleed measles patients. These assertions are readily countered by the following facts. Tuberculosis in children after measles is common probably only because of their debilitated condition, and is not due to any specific predisposition. Nevertheless, we have taken our bloods almost entirely from adults, who do not develop tuberculosis as do children. Further, the precautions taken in phenolizing and passing through a bacterial filter render the serum sterile, and these should satisfy even the most sceptical. Professor Kraus of Vienna has examined by animal inoculation many specimens of convalescent measles serum which had not been treated with the double precautions mentioned above, and he has never yet thereby produced a tuberculous lesion in a guinea-pig. As the serum is of human origin anaphylaxis or serum reactions do not occur. The serum can be used so as to give different results, and these depend on the stage of incubation at which the injection is made. Copeman's ideas upon the inoculation period of measles are as follows:

In order to achieve complete protection the serum should be injected before the fifth or sixth day of incubation. This is called "sero-prevention," and results in a passive immunity which lasts roughly a month. From the sixth to the ninth day the serum does not protect fully, but allows only a very mild attack of measles to ensue. To this the term "sero-attenuation" is applied. There is a moderate attack, with the establishment of active immunity. After the ninth day we cannot hope for any benefit from serum. Injection on the tenth day produces Debré's phenomenon, a local blanching at the site of injection. Epidemiologically the attenuated attack is the best result that can be obtained, as it confers on the individual a permanent active immunity, whereas in the case of a patient who has been completely protected he has only a temporary passive immunity lasting two to four weeks. From the practical point of view it is clear that in institutional work one must always aim at complete protection, whereas in private practice, where it is only the individual who has to be considered, the best result is a mild or aborted attack. Of course, where a desperately ill child has been exposed to measles we must at all costs prevent the attack, and it is advisable to use a slightly larger dose, and to administer it as early as possible in the incubation period. The attenuated attack is indeed an extremely mild affair. Some cases exhibit a small bout of pyrexia to 100° F. for a day or two about the fourteenth day of incubation; others vary from a few measly spots over the trunk (apyrexial) to a typical attack of measles with coryza and bronchitis, which has all subsided in from twenty-four to forty-eight hours. We have never seen Koplik's spots in any of these measles cases after convalescent serum has been given. A very common feature is a prolonged incubation period—in some cases even as long as twenty-six days—followed by a mild measles. There is no doubt that from a hospital administrative point of view this can be rather disturbing, as it holds a ward in quarantine for over three weeks. If, however, all new admissions to the ward are given serum, this in no way hinders the work of the ward, which may continue its normal routine.

*Dosage*

Originally we used 3 c.cm. for children up to 3 years and 5 c.cm. for children over 3. This has never been strictly adhered to, as we increase the dose for big children and for adults, and also if the incubation is well advanced. We have now increased our doses to 5 and 7 c.cm., and

believe that this is a more adequate and satisfactory dosage. All the injections are made intramuscularly into the buttock. Serum has been tried in treatment of severe measles without success, because the antibody content is not sufficiently high and enormous doses would be required to have any effect. For the same reason the serum is of no value for the blanching of a rash, although it is sufficiently strong to prevent the appearance of the rash in an area if injected before the rash appears generally (Debré's phenomenon). Whole blood may be used instead of serum, and in this case the blood of a convalescent is injected intramuscularly into the recipient, the dose being double the serum dose.

*Results*

At the Paris Clinic, where an enormous number of children have been treated, Debré reports 80 per cent. protection. Gunn reports 95.7 per cent. complete protection, and of his 5 failures 3 were injected on the first day and two on the eighth day. The two latter doses were, of course, given too late for complete protection, and the other three cases were so mild as to be hardly recognizable as measles. Our own series now amounts to 586 cases, of which 461 were injected by us at the Children's Hospital following ward infections, and 125 were cases from practitioners in various parts of the country following home or hospital infections. In the hospital series there were 14 failures, or 3 per cent., and the outside cases 7 failures, or 5.6 per cent. As we have already noted, the "failures" in both series include several injected after the fifth day, and are almost all extremely mild cases.

*Analysis of Twenty-one "Failures"*

Serum Injected	Aborted	Mild	Normal	Severe	Total
Before fifth day of incubation	3	3	4	0	10
Sixth to tenth day ... ..	1	9	1	0	11*
Totals ... ..	4	12	5	0	21

\* It should be noted that these 11 cases should really be omitted, as they are examples of late inoculations where a mild measles is to be expected. Of the 10 before the fifth day 6 were so mild as hardly to be recognized as measles.

*Controls*

It is a matter of some difficulty at the moment to obtain satisfactory controls. It is almost impossible to say how many children in an infected ward would develop measles if not inoculated, but it is very common for several patients to contract measles within a fortnight. We can show several such wards, quite typical and representative of many, in which within fifteen to sixteen days four or five children of varying ages have contracted measles, and in some the infection has then recurred so often as to necessitate closing the ward. Furthermore, we should really know how many patients have previously had measles, but this again we think can be assumed to be, in the same hospital over a prolonged period, a constant figure. Even a previous attack, of course, does not necessarily confer an immunity, and one of our cases, in spite of an undoubted history of measles plus a dose of convalescent serum, developed a mild measles fourteen days after exposure.

Gunn, working at a fever hospital, particularly with cross-infections, had ample opportunities for controls. His series included wards which were uninoculated, wards inoculated with various animal serums, and wards protected with convalescent serum. His 95.7 per cent. protection, together with our final figures of 98.3 per cent., afford very striking and sufficient proof that until an efficient animal serum is prepared convalescent measles serum is the only weapon we have for preventing measles, and it should be more widely used than it is at present.