

streptococcus does not preclude its accounting for the exanthem in the human case of the disease, or the "skin-reaction" in the non-immune. Even if scarlet fever is a localized infection caused by a specific streptococcus, the organisms are constantly dying, and consequently an endotoxin is liberated which eventually must reach the cutaneous tissues.

In human scarlet fever the nephritis is constant and often the outstanding feature of the disease. The glomerular lesion in the kidney is almost pathognomonic of human scarlet fever; so much so that we are inclined to regard the toxic excitant as one having a special predilection for the kidney. We have been successful in the production of a glomerular nephritis in the rabbit with *streptococcus scarlatinae* lysate.

## 3202

### Studies upon the virus of measles

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It is generally accepted that the symptom-complex of measles, including the exanthem and the enanthem, may be experimentally induced in the monkey, rabbit and guinea pig with either the filtrate (Berkfeld N.) of blood or naso-pharyngeal secretion from cases of human measles. The transmission experiments of Hektoen,<sup>1</sup> Goldberger and Anderson,<sup>2</sup> Blake and Trask,<sup>3</sup> Duval and D'Aunoy,<sup>4</sup> and others, have established that the causal excitant of measles is transmissible from man to lower animal, is filterable and exists in the circulating blood during the febrile stage of the disease. Although the virus of measles can be propagated in certain of the lower animals, its cultivation *in vitro* has not been definitely established. Of the various cultures reported

<sup>1</sup> Hektoen, L., *J. Infec. Dis.*, 1905, ii 238.

<sup>2</sup> Goldberger, J., and Anderson, J. F., *J. Am. Med. Assn.*, 1911, lvii, 971.

<sup>3</sup> Blake, F. G., and Trask, J. D., *J. Exp. Med.*, 1921, xxxiv, 385.

<sup>4</sup> Duval, C. W., and D'Aunoy, R., *J. Exp. Med.*, 1922, xxxv, 257; xxxvi, 231.

those of Tunnicliffe,<sup>5</sup> and Caronia<sup>6</sup> are entitled to special consideration.

With certain facts before us as a working basis, attempts were made to learn more about the nature of the measles virus; our first objective being its cultivation outside of the living host. For this purpose a variety of special as well as ordinary culture media was employed. The different media were inoculated with the filtered and unfiltered virus-blood from human measles and from the experimentally infected rabbit. Duplicate cultures were maintained under aerobic and anaerobic conditions, and incubated at a temperature of 37° C. for periods of ten days. At such times the cultures were carefully examined microscopically for growth. One mil quantities of cultures that were suggestive of growth were subplanted, and at the same time a like quantity was injected intravenously into normal rabbits. These animals were inoculated in order to determine whether the *in vitro* virus was infectious. The leucocytes and daily temperatures of these rabbits were carefully noted for reactions over a period of fourteen days.

Rabbits injected intravenously with one mil quantities of semi-solid plasma hydrocele Ringer cultures of the second, third and fourth generations reacted in a characteristic manner, *i. e.*, marked drop in the circulating leucocytes and elevation in the temperature following an incubation period of eight to twelve days. The reaction in the rabbits was identical with that induced by the injection of five mils of freshly drawn human measles blood. Here it is significant that rabbits receiving five mils of human virus blood which had been kept for two weeks at ice-box temperature failed to react. These experiments not only prove that the measles virus retains its power to infect after a relayed sojourn in hydrocele or semi-solid plasma media for a period of forty days at 37° C., but suggests that it multiplies under certain *in vitro* conditions. Since a fourth subtransplantation represents a great dilution of the original virus planted, we believe that the reaction in the animals was the result of virus numbers rather than individual virus virulence. Furthermore when the blood of rabbits which reacted to culture inoculations was injected into other rabbits these reacted similarly.

While no macroscopic growth was visible for the initial cul-

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<sup>5</sup> Tunnicliffe, R., *J. Am. Med. Assn.*, 1917, lxviii, 1028.

<sup>6</sup> Caronia, *Pedicatia*, 1923, xxxi, 801.

tures or for the subsequent transplants, on careful microscopic examination there was noted in culture tubes that contained semi-solid plasma or hydrocele fluid, an occasional small Gram positive coccus. The microorganism occurred single, in pairs and short chains. Subsequently a good growth of this coccus was obtained upon ordinary blood agar slants, and under aerobic conditions at 37° C. incubation. A comparative cultural study of the various isolations revealed their complete correspondence with one another and the coccus described by Tunnicliff. In this connection it should be mentioned that in a previous study upon the transmission of measles, one of us (Duval) had noted a small Gram positive coccus in certain of the tubes of Noguchi's semi-solid medium which had been inoculated with unfiltered human measles blood. At that time the coccus was considered a contaminator and no further attention was paid to it, mainly because it occurred in cultures that had been inoculated with unfiltered measles blood and the organism appeared too large to pass through filters.

It is to be said of this coccus isolated by us from human measles blood and also of the Tunnicliff coccus that young rabbits react characteristically to intravenous injections. Cultures of the coccus were recovered from the blood of the reacting rabbits ten days after the inoculation. While no exanthem or enanthem was noted in these reacting animals, a marked concomitant leucopenia and pyrexia regularly occurred after an incubation period of seven to eight days. In regard to filterability, Tunnicliffe claims that her culture is filterable; however, she does not say under what cultural conditions; neither the coccus isolated by us from measles blood nor the coccus of Tunnicliffe when cultured aerobically will pass through the Berkfeld N or V filters. The culture filtrates fail to give rise to a reaction in the rabbit or growth upon any nutrient medium. This is significant in that it favors a causal rôle for the coccus to the exclusion of a filterable microorganism growing in association with the coccus. However, both organisms are filterable from cultures that are grown anaerobically. Under this and other abnormal growth conditions the coccus is extremely small compared to its size in cultures of favorable environment.

#### SUMMARY.

The causal excitant of measles exists in the circulating blood during the febrile stage of the disease. The Berkfeld filtered virus

blood induces in the monkey, rabbit and guinea pig the symptom complex of human measles.

A living agent capable of causing in the experimental animal a concomitant leucopenia and pyrexia may be propagated and subcultured *in vitro* through several generations upon hydrocele or semi-solid plasma Ringer medium. In the cultures prepared from the unfiltered human measles blood of reacting animals there frequently occurs a small gram positive coccus, which in subplants to blood agar medium grows readily and under aerobic conditions. Cultures of this coccus are likewise capable of inducing in the rabbit a leucopenia and pyrexia following an incubation period of seven to eight days. The coccus culturally and tinctorially corresponds to the culture reported by Tunnicliff. Since the coccus was cultured from the unfiltered measles blood, we prefer to reserve opinion at this writing regarding its significance in measles.

### 3203

#### **The heart of the racing greyhound. Hypertrophy of the heart.**

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The effect of strenuous competitive athletics on the heart, that is, the question of true physiological work hypertrophy, is a matter of considerable interest. A study, therefore, of the heart of the greyhound was undertaken. The hearts and body weights of ten of these thoroughbred dogs have been studied and compared with the established normal heart-weight-body-weight ratio of .00798 or 7.98 grams of heart per kilogram of body weight, for ordinary mongrel dogs.<sup>1</sup> The largest heart was found in the oldest and most successful racer, "Victorious Red," aged three years, with a ratio of 17.3. Five greyhounds that had had their schooling, whose age was about two years and who had raced not more than three times, ranked according to ratio as follows:

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<sup>1</sup> Herrmann, George R., *Am. Heart J.*, 1925, i, 213.