

considerably increased, but the increased activity required of the heart exposes it to the danger of insufficiency of its action. This in many cases leads to a fatal termination."

In the passage just quoted there are many contradictory statements which seem to indicate some deplorable misconceptions, and lest it might be thought that my friend and colleague, Dr. Bruce, is in any degree responsible for the singular confusion of ideas pervading the passage, it is only right to say that his translation has been executed with a fidelity worthy of a better cause. "During life," says Professor Thoma, "the diminution of the elasticity of the arteries shows itself by a soft, distensible pulse and a sphygmographic tracing with a very high dirotic rise, which is unduly far removed from the apex of the wave. The distance of the apex of the dirotic rise from that of the pulse wave indicates in these conditions that the pulse wave is somewhat slowly propagated in the blood stream." Such a statement as this deserves the closest examination. It seems as if the author judged elasticity, not by the amount of strain which can be borne and restitution pressure produced, but solely by the amount of resistance to stress. As we have already seen, Professor Roy and other workers in this field correctly measure elasticity by the amount of distortion which can be undergone, followed by return to normal form; and how a soft, distensible pulse and a sphygmographic tracing with a very high dirotic rise can be produced by a diminution of the elasticity of the arteries entirely passes my comprehension. Again, let us hear Professor Thoma. "Lastly," he says, "I may point out that in many cases the appearance of a pulse in the retinal arteries on ophthalmoscopic examination is to be ascribed to a diminution of the elasticity of their wall." Here the author is on safer ground, but he happens to have crossed to the other side of the hedge from that on which he stood when we compare the first passage referred to with that just quoted. The appearance of a pulse in the retinal arteries shows that the arterial system is either somewhat like a system of rigid tubes with an intermittent flow, or it exemplifies the point made out by Roy, previously referred to, that the arterial system is too wide for the quantity of blood.

But these are minor degrees of misconception when compared with an astounding statement which follows. "In consequence," the author states, "of the great distension to which the weakened walls of the arteries and veins are subjected by the blood-stream their lumen dilates. Since, however, the amount of blood which flows from a section of an artery in a given time is determined chiefly by the condition of the capillaries, the widening of the arteries only produces a moderate increase in the amount of blood which flows through, so that at the same time the rapidity of the blood-stream is reduced in the widened vessel. A retardation of the stream is produced, and this, as I have been able to show, is the immediate cause of a new formation of connective tissue in the intima of the widened artery. This again diminishes the lumen of the artery, and the latter is thus re-adapted to the blood stream. The new formation of the connective tissue in the intima renders the vessel more firm, so that it appears more rigid and less yielding. The elasticity of the wall of the vessel, and therefore the resistance which it offers to stretching, is considerably increased, often to such an extent that the pulsatile movements within it are reduced." The perusal of this amazing statement must leave the reader in a condition little less than pitiable. He will infallibly be left in doubt whether the author or himself has been deprived of the faculty of reason. Professor Thoma assuredly "walketh in a vain show." How, in the name of everything that is reasonable, can the elasticity of the wall of the vessel be increased by a new formation of connective tissue rendering the vessel at once more rigid and less yielding?

In what has been said it has been my endeavour to keep well within the limits of a just and even generous judgment. My own tendencies are at all times more appreciative than critical, yet, while fully recognising the great services to circulatory pathology rendered by Professor Thoma, it seems my bounden duty to point out what is certainly a grave misconception of physical facts as well as an unfortunate misuse of physical terms. The passage which has been arraigned forms a curious commentary upon a sentence in the author's preface. "Since the beginning of my career," Professor Thoma says, "I have endeavoured to investigate the mechanical laws which govern pathological processes, and accordingly have spent much time in the preliminary study of mechanics and mathematics." It is indeed difficult to reconcile this autobiographical statement with the results

specially referred to. In the preceding criticism there has been no intention on my part to scoff at the unfortunate blunders which have been criticised. "A smile for a friend and a sneer for the world"—the motto assumed for the youthful hero of romance by a gifted author¹³—may be a useful rule in the field of politics, but it has no place in science, for in all our discussions and controversies our sole aim is to arrive at the truth.

Edinburgh.

PRELIMINARY NOTE ON THE USE OF THE AGGLUTINATIVE ACTION OF HUMAN SERUM FOR THE DIAGNOSIS OF ENTERIC FEVER.

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IF a drop of an emulsion of a motile pathogenic organism be mixed with a drop of the serum of an animal immunised against this particular bacillus the micro-organisms collect together in "clumps" and lose their mobility. The importance of this reaction, which had been seen by others, was first recognised and studied by Gruber and Durham. They threw out the suggestion that it might be made of diagnostic value in the sense that bacteria cultivated from the stools of cholera or typhoid fever patients might be identified by its aid. But it appeared likely on *a priori* grounds that the "agglutinines" found in the serum of immunised animals would also be formed in the human body during an attack of enteric fever or cholera (it being already known that "protective" substances, at any rate, are so formed); and at Professor Gruber's suggestion I undertook the investigation of this point as part of the question whether immunity and protection are not (in certain diseases) dependent on and proportional to the agglutinines present. The serum of normal guinea-pigs has rarely any pronounced agglutinative action, but it does not follow that the same would hold good for man, and an examination of some thirty cases of normal and diseased individuals, of whom more details are given below, showed the presence of agglutinines in persons not suffering and not having suffered from enteric fever (or cholera). Although anticipating matters, it may be here stated that hitherto it is only in cases of enteric fever that the serum shows a distinct agglutinative action within thirty minutes when diluted sixteen times, and hence this reaction can be used as a diagnostic sign. If the reaction occur in still greater dilution its diagnostic value is correspondingly increased. Enteric fever is fortunately rare in Vienna, so that this positive result was obtained in only eight cases, but the negative result in all the others seems sufficient to justify its publication in order that it may receive its corroboration or otherwise from other observers.

Practically, the method pursued is as follows. A drop of blood is taken either from the ear or the finger in an U-shaped capillary tube and centrifugalised. The tube is broken off at the junction of serum and corpuscles and the drop of serum blown out on to a glass slide. The necessary quantity is sucked up to the first mark on a straight capillary tube having another mark corresponding to sixteen times the volume at the first mark. Bouillon is then sucked up with the serum until the second mark is reached, the whole blown out on to a glass slide, mixed and again sucked up, and the process repeated two or three times to ensure thorough mixing. The emulsion of typhoid fever bacilli is prepared by taking a small platinum loopful of a culture not more than twenty-four hours old and grown on rather dry agar, and carefully rubbing it up against the side of a glass capsule containing 1 cm.³ of bouillon, with a drop of the bouillon, and subsequently mixing it with the whole quantity. A control preparation of this must be examined under the microscope to make certain that there are no, or very few, pre-existent clumps in the emulsion. A small drop of the diluted serum is then placed on a cover-glass, a drop as near as possible of the same size from the "typhoid emulsion" mixed with it, the cover-glass placed on a vaselined hollow slide, and the mixture examined as a hanging

¹³ Lord Beaconsfield: Vivian Grey, Book ii., Chap. iii.

drop, with an immersion lens. Under the microscope it will be seen that the bacilli gradually form groups of three or four, which, by the addition of other bacilli, constantly increase in size until the majority are in "clumps" with impaired or lost motility. If the reaction is marked within thirty minutes the case is one of enteric fever, but without greater experience it is impossible to say that the absence of the reaction negatives such a diagnosis. In any negative result more than one examination should always be made, for it occasionally, although rarely, occurs, probably from experimental errors, such as varying quality of bouillon, &c., that the reaction is seen on one day and not on another. And it has happened in one case, in which the typhoid fever bacilli were cultivated from the blood, that the reaction was better marked in greater dilution. Complicated as the reaction may read it is really quite simple of performance and takes very little time.

The serum of man is very variable both as regards the power and the kind of agglutinines present under ordinary conditions. Excluding the cases of enteric fever, 32 specimens of serum were examined, of which 9 were from normal individuals (3 of whom, however, had had enteric fever) and 23 from cases of various diseases. Typhoid fever bacillus was acted on in 28 cases out of 37, in 13 markedly; 5 cases had had enteric fever from five to thirty-seven years previously and 8 were suffering from it. Cholera bacillus was acted on in 16 cases out of 29, in 9 markedly. Only 1 patient had previously had cholera. Coli bacillus was acted on in all 3 cases examined. In 2 of these 3 typhoid fever bacillus was also acted on. In the following table these results are better seen:

Disease.	Previous typhoid.	Action.		
		Typhoid.	Cholera.	Coli.
Chronic rheumatism ...	*	†	†	—
Phthisis (acute)	*	—	*	—
Cirrhosis, icterus	*	†	†	†
Phthisis	*	—	*	—
Meningitis	? 4 years ago.	†	†	—
Typhoid (27th day)	—	† (1/2)	†	†
Typhoid (17th day)	—	†	—	—
Phthisis	*	*	†	†
Bronchitis	*	†	†	—
Typhoid (11th day)	—	† (1/10)	†	—
Icterus	*	†	†	—
Normal	*	*	*	—
Normal (placental blood) ...	5 years ago.	†	*	—
Normal ,, ,, ...	*	†	†	—
Normal ,, ,, ...	*	*	*	—
Hemiplegia	30 years ago.	† (1/4)	†	—
Normal	37 years ago.	† (1/4)	†	—
Icterus	*	†	†	—
Tetany	*	†	†	—
Carcinoma	*	†	*	—
Gastric ulcer... ..	*	†	—	—
Septicæmia	*	†	†	—
Chronic renal	*	† (1/4)	*	—
Carcinoma icterus	*	† (1/4)	*	—
Syringomyelia	18 years ago.	† (1/4)	*	—
Normal (maternal blood) ...	*	*	*	—
Cirrhosis icterus	—	† (1/4)	*	—
Normal (placental blood) ...	10 years ago.	†	*	—
Normal (maternal blood) ...	*	† (1/4)	† (1/4)	—
Normal (placental blood) ...	*	*	†	—
Normal (maternal blood) ...	*	† (1/4)	—	—
Normal (placental blood) ...	*	*	—	—
Normal (maternal blood) ...	*	† (1/4)	—	—
Normal (placental blood) ...	*	—	—	—
Typhoid (10th day)	—	† (1/4)	—	—
Typhoid (13th day)	—	† (1/4)	—	—
Typhoid (21st day)	—	† (1/4)	—	—
Typhoid (26th day)	—	† (1/4)	—	—
Typhoid (33rd day)	—	† (1/12)	—	—
Chronic rheumatism	*	*	—	—

EXPLANATION OF SIGNS.—* = no action. † = fair or distinct action.

† = marked action. The fractions indicate the greatest dilution in which the action was still distinct. Actually the dilution is double, through an equal quantity of emulsion being added.

The greater strength of the serum of enteric fever patients is thus very evident. Several specimens from each patient were examined, and although the power gradually diminished it was always still considerable when the patient was discharged. The cases in which jaundice is present yield a serum which, undiluted, has an action often as rapid and complete as an enteric serum; but the falling off in strength is quite out of proportion to the dilution, so that it is impossible to tell what degree of dilution a serum will stand from the initial intensity of its action. Moreover, jaundice is almost unknown in enteric fever.

Although no opportunity presented itself for examining a case of acute miliary tuberculosis, the case of fairly extensive phthisis with high fever gave no reaction, and the case of meningitis only a slight reaction, so that these two diseases for which enteric fever is liable to be mistaken do not, *per se*, seem likely to cause confusion in the serum test. It is interesting to note the different action of the maternal blood (obtained after separation of the placenta) and of the placental blood, especially in view of the general absence of hereditary immunity to infectious diseases. By the examination of a larger number of ordinary cases as well as of cases of enterica, at this season gradually becoming more numerous, I hope soon to present further evidence in support of the above test; in the meanwhile I commend it to the favour of others who may have the opportunity of applying it, especially in early cases.

Whilst this work was in progress a short communication by Widal applying a similar method macroscopically has been published in the *Semaine Médicale*. It requires, however, a larger quantity of blood and a longer time, and apparently, from the rather meagre description, a final resort to the microscope; and in one case, at any rate, I was unable to detect the reaction.

Vienna.

ON THE ASSOCIATION OF SEROUS HÆMORRHAGES WITH CONDITIONS OF DEFECTIVE BLOOD-COAGULABILITY.

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IN previous papers I have pointed out that, on the one hand, excessive hæmorrhages from trifling wounds, and, on the other hand "spontaneous hæmorrhages," are in almost all cases attributable to a defect in blood-coagulability. The epistaxis and hæmorrhage from the bowel in typhoid fever, the epistaxis of growing children, and the excessive hæmorrhages of hæmophilic patients are typical instances of hæmorrhages which are due to this cause. Conditions of deficient blood-coagulability do not, however, manifest themselves only in a tendency to "actual hæmorrhages." They manifest themselves also in a tendency to increased transudation of plasma through the capillary wall—i.e., in a tendency to "serous hæmorrhages." I propose here to review the more important varieties of such "serous hæmorrhage" and to draw attention to the association of each of these forms of serous hæmorrhage with conditions of diminished blood-coagulability.

Serous hæmorrhage in the skin.—I have elsewhere¹ shown that urticaria or serous hæmorrhage into the skin is often associated with, and is probably dependent upon, a condition of defective blood-coagulability. In particular I have pointed out that this holds true (a) of the urticarias which supervene upon the injection of diphtheria antitoxin; (b) of the urticarias which supervene upon eating acid fruit; and (c) in all probability also of the urticarias which supervene after eating crabs or shellfish.² Two other urticarias—i.e., the urticarias which supervene occasionally after eating rhubarb and the urticaria which supervenes, more exceptionally, after the administration of soap enemas—

¹ THE LANCET, Jan. 18th, 1896; British Journal of Dermatology, No. 89, vol. viii.

² Since writing the above this inference has been confirmed by observations made by Dr. Wm. John Scott on a case of shell-fish urticaria, which was successfully treated by him with calcium chloride.