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J. A. SHAW-MACKENZIE AND O. ROSENHEIM

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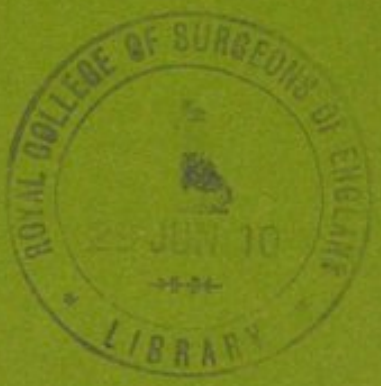

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A Lipoclastic accelerating Action of Serum as an Index in Pathological Conditions.[1]

By J. A. Shaw-Mackenzie and O. Rosenheim.[2]

Investigating the lipolytic (preferably termed the lipoclastic) activity of serum, we were able to confirm previous statements on the subject, that a true fat-splitting enzyme does not occur in serum, whilst even the action of what might be called a butyrase on the esters of lower fatty acids is a feeble one. During the course of this work, however, we made the observation that serum, although not possessing any fat-splitting action by itself, nevertheless increases in a remarkable way the activity of pancreatic lipase contained in pancreatic extracts as well as in pancreatic secretion. This property is possessed to a greater or less degree by all the animal sera which we have examined—namely, horse, ox, pig, dog, cat, rat, mouse, rabbit, marmoset. This accelerating action of serum is not specific, in so far as the lipolysis by pig's lipase is increased in the same way by the addition of pig's serum, as well as by that of other animals, whilst, on the other hand, the lipase of the ox is acted upon also by the serum of the pig.

On examination of normal human serum we found that its accelerating power, as compared with the same quantity of animal serum, is about half of the latter. In certain pathological conditions, however, this reaction is increased to double, and even four times, that in health.

[1] Read at the laboratory meeting of the Section at King's College, March 1.

[2] From the Physiological Laboratory, King's College, London.

[In addition to serum we also examined the cerebrospinal fluid of the dog and cerebrospinal fluid from cases of general paralysis, which were found to be practically inactive. Serous effusions, so far examined, have shown the reaction to a marked degree. We examined also a series of press juices of various animal organs, and found (in the absence of a lipoclastic action of the juice itself) an accelerating action in the case of the testicle and thyroid, whilst in the case of the duodenal press juice the result corresponded to the sum of the lipoclastic action of pancreas and duodenum. In the case of glycerine extracts, those of the testicle, thyroid, ovary, and spleen were found to be slightly active, whilst no acceleration was observed in the case of glycerine extracts of lymphatic glands and prostate.]

With regard to the chemical nature of this accelerating substance in serum very little can be said at present. It withstands the temperature of boiling water; it is not destroyed by putrefaction; it dialyses and is soluble in dilute alcohol. An important property of the accelerator was brought to light by the investigation of its behaviour towards cholesterin, which in all cases was found to exert an inhibitory action.

Details of the method of obtaining a pancreatic extract rich in fat-splitting properties, the various substances which accelerate this action still further, together with the inhibitory action of cholesterin on all of these, have been communicated elsewhere and will be published shortly. Briefly, however, it may be stated that the lipoclastic action is estimated by the amount of decinormal potash used for the neutralization of the fatty acids set free by pancreatic lipase acting on olive-oil emulsion, or on ethyl butyrate, the mixture being incubated at a temperature of 37° C. for a certain time.

By adjusting the conditions of the experiments in such a way as to reduce the amount of pancreatic lipase and olive-oil emulsion (or of ethyl butyrate) to a minimum, we have been able to show the accelerating power of as little as 0·1 c.c. of serum. Generally, 0·25 c.c. and 0·5 c.c. of serum are sufficient. In this way one is able to compare the degree of acceleration of serum in health and disease. As a matter of fact our first observation on this accelerating reaction was made in a case of carcinoma.

Taking normal human serum as a basis of comparison, the following figures give the results in a typical case: 0·25 c.c. of glycerine extract of pancreas, 0·5 c.c. of water and 2·5 c.c. of olive-oil emulsion were mixed, and after incubation the amount of acid liberated required 5·3 c.c. of decinormal potash to neutralize it. When 0·1 c.c. of serum had been added, this figure rose to 7·4; when 0·25 c.c. serum was added, it

increased to 8; and when 0·5 c.c. serum was added, it rose to 9·7. Or in tabular form:—

TABLE I—AVERAGE NORMAL SERUM.

	c.c. $\frac{N}{10}$ KOH	Acceleration
Pancreatic extract alone	5·3 ...	—
Addition of serum, 0·1 c.c.	7·4 ...	+ 2·1
,, ,, 0·25 c.c.	8·0 ...	+ 2·7
,, ,, 0·5 c.c.	9·7 ...	+ 4·4

The following tables summarise our results when we investigated in a similar way the action of serum and serous effusions from pathological cases. Table II gives results with serum from cases of carcinoma, Table III those with serum from non-malignant cases, Table IV those with serous effusions in carcinomatous and non-malignant cases. The first of these was œdema fluid from the arm, and the remainder ascitic fluids. In these cases the amount of fluid available was larger than with serum, and the figures are proportionately higher.

TABLE II—SERUM IN CARCINOMA.

Case	Serum added	Acceleration
Recurrent carcinoma; breast	0·25 c.c. ...	+ 13·7
Carcinoma of rectum	0·25 c.c. ...	+ 7·5
	0·5 c.c. ...	+ 11·8
Carcinoma of stomach	0·25 c.c. ...	+ 4·9
	0·5 c.c. ...	+ 10·6
Recurrent carcinoma; breast	0·25 c.c. ...	+ 5·2
	0·5 c.c. ...	+ 9·2
Recurrence of carcinoma of neck ...	0·07 c.c. ...	+ 7·2

TABLE III—SERUM IN NON-MALIGNANT DISEASE.

Case	Serum added	Acceleration
Syphilis, under treatment, one year ...	0·25 c.c. ...	+ 4·6
	0·5 c.c. ...	+ 5·9
Glycosuria	0·1 c.c. ...	+ 5·6
	0·25 c.c. ...	+ 8·1
	0·5 c.c. ...	+ 10·6
Tabes	0·5 c.c. ...	+ 16·2

TABLE IV—SEROUS EFFUSIONS (CARCINOMA AND NON-MALIGNANT).

Case	Fluid added	Acceleration
Œdema of arm, secondary to recurrent carcinoma of breast	2·5 c.c. ...	+ 12·3
Ovarian, malignant tumour	2·5 c.c. ...	+ 33·0
Peritoneal carcinoma	5·0 c.c. ...	+ 27·3
Ovarian, malignant tumour	5·0 c.c. ...	+ 26·8
Cirrhosis, liver (non-malignant)	5·0 c.c. ...	+ 34·1
Cirrhosis of liver ? (non-malignant)	5·0 c.c. ...	+ 20·1

It may be mentioned also that in some of the sera as used for therapeutic purposes a lipoclastic acceleration was observed. For example, 5 c.c. of added antidiphtheritic horse serum gave an acceleration of + 14·6, and 5 c.c. of normal horse serum + 27·1.

It will therefore be seen from the experiments that carcinoma is not the only pathological condition in which the lipoclastic acceleration of serum occurs.

Some fifteen months ago Professor Halliburton kindly afforded one of us (J. A. Shaw-Mackenzie) the opportunity of working in the physiological laboratory of King's College on the tryptic or antitryptic power of the blood, more especially in relation to carcinoma. According to experiments performed concurrently with the lipoclastic investigations, it may be stated that the antitryptic power of serum would seem to run parallel with the lipoclastic acceleration, in normal and carcinomatous conditions. But in the non-malignant cases so far examined, which show an increased lipoclastic acceleration, the antitryptic power would seem to be normal. Many more observations, however, appear necessary before one can state definitely that this is a general rule.

We desire to express our thanks to those who have kindly provided us with specimens in this preliminary inquiry—Dr. J. C. Matthews, Dr. R. H. C. Gompertz, Dr. F. W. Mott, Dr. E. L. Holland, Sir A. Fripp, Dr. Vernon Jones, Staff-Surgeon J. R. Muir, R.N., Dr. Porter Parkinson, Dr. W. E. Dixon, Surgeon D. P. Chapman, R.N., Dr. B. Hughes, and Dr. J. D. McCulloch.

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