

ON THE CAUSE OF DEATH AS DETERMINED BY MICROSCOPICAL EXAMINATION IN THREE ANIMALS KILLED IN THE COURSE OF "SATURATION" TESTS.

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A Report to the Medical Research Committee.

IN a paper by Capt. Ainley Walker in this *Journal*¹ reference is made to three experiments on three rabbits killed by the "saturation" method of Lieut.-Colonel Gordon which consists in injecting into the auricular vein slope cultures of organisms in massive doses at frequent intervals. The organisms used in the present experiments were the Meningococcus, *B. typhosus*, and *Sarcina lutea*. Capt. Ainley Walker has handed over to me the organs of the rabbits used for histological examination as to any evidence that might exist of the cause of death. The organs had all been fixed in alcohol. Portions of each were cut out and embedded in the usual way in paraffin. The sections made were stained by haematoxylin and eosin and by such other methods as the appearances suggested. It will be best to set out in detail the features of each organ and then to summarise the whole at the end.

(1) RABBIT KILLED BY "SATURATION" WITH MENINGOCOCCUS CULTURE.

Lung. In all sections there are several patches of haemorrhage. The arteries are either empty or contain small portions of massed red cells and there are a larger number of leucocytes than normal. The intima shows swelling and proliferation of cells. The periarterial lymphatics are distended with blood. The bronchi show slight epithelial catarrh. The veins contain much clot and some of the smaller ones are turgid with clot that contains many leucocytes. The capillaries everywhere contain leucocytes and endothelial cells but very few red cells are seen. In many can be seen plugs of fibrin which is very clearly seen by the low power in any section of the lung stained by Weigert's fibrin method, the deep blue dots and tags of fibrin standing out against the

¹ E. W. Ainley Walker, *Journal of Hygiene*, Cambridge, 1918, Vol. xvii. p. 389.

red of the carmine used as a counterstain. Some of these plugs can be found partially extruded into a vein.

Kidney. Normal in general. Round cells are numerous in the capillaries and glomeruli where an occasional embolus is seen. Catarrh is present in the arterial intima. Weigert's stain shows glomeruli that contain fibrinous clot in some of their capillaries.

Liver. Early fatty infiltration. Round cells are present in capillaries. A few rounded emboli are seen in the capillaries and numerous filaments of fibrin stretching in their lumina and in some instances completely filling them.

Suprarenals. Some fibrinous emboli and fibrinous strands in the capillaries.

(2) RABBIT KILLED BY "SATURATION" WITH *B. TYPHOSUS*.

Lung. The description for meningococcus is the same as that for Typhoid except for a diminished intensity of the process. Gram negative bacilli often as diplo-bacilli can be seen in the capillaries and in the veins of the neighbourhood of the leucocytes.

Suprarenal. Some capsular haemorrhage otherwise nothing abnormal.

Liver. A good deal of fibrin of loose texture in capillaries. Under an oil immersion single threads can be seen lying on many capillaries. A few obvious fibrinous emboli, of looser texture than in meningococcal liver.

Kidney. A very few small fibrinous emboli in the capillaries of the glomeruli and a few strands of fibrin also in some of the veins, otherwise no great abnormality.

Heart. The coagulated blood (red clot) in the left ventricle shows numerous fibrinous emboli around one or more leucocytes. No emboli seen in heart substance.

(3) RABBIT KILLED BY "SATURATION" WITH *SARCINA LUTEA*.

Lung. Most of the larger veins show a mass of clot slightly shrunken away from the walls, white mixed, and red, with large numbers of polymorphs in the white parts. These show small collections of cells which presumably have been disgorged from the capillaries. The arteries are empty for the most part but contain portions of fibrinous clot; but the most marked feature is the enormous dilatation of the periarterial lymphatics which contain fibrinous red clot. Many arteries show marked acute intimal swelling.

There is a marked collection of polymorphs in the capillaries which for the most part contain but few red cells, in fact they are choked with polymorphs and plugs of fibrin which can be well seen in a fibrin stained preparation. Shaggy small fibrinous clots are contained in the alveoli which are otherwise empty, but a few are filled with blood. Numerous capillary emboli are seen in the Weigert stained sections. Organisms are seen embedded in fibrinous emboli though some care is necessary in detecting them.

Kidney. Most of the veins show recent fibrinous, mixed or red clot. The fibrinous clot shows a high proportion of leucocytes, and in the recent red clot are to be seen portions of fibrinous clot which have obviously been formed at some earlier period. The clot does not completely fill the lumen, suggesting a retraction from the original bulk. The larger arteries are either empty or contain some fibrinous clot. The glomeruli are diminished in size and show a marked space between glomeruli and Bowman's capsule, their capillaries as shown by Weigert's method contain fibrin and some red cells but are only poorly filled. The convoluted tubules show slight catarrh. In the general capillaries there is hardly any blood. Some glomeruli are hardly affected, in others the capillaries are nearly all plugged with fibrinous emboli.

Liver. The hepatic and portal veins are filled with clot, white, red or mixed, the fibrinous portions of the latter showing many leucocytes. Many of these portions are obviously emboli from fibrinous clot in capillary vessels. The capillaries contain numbers of polymorphs but red cells have to be carefully sought for. A Weigert stained preparation shows numerous fibrinous embolic plugs, tags and strands in the capillaries.

Suprarenals. Haemorrhage showing thrombosis just exterior to the capsule. The capillaries contain some fibrin and sarcinae but very few normal red cells.

The veins of the medulla contain white or red clot.

Brain. Nil.

REMARKS.

It will be evident from a perusal of the foregoing details that all three animals present the same features. In the lung there is a widespread capillary embolism which has led to haemorrhage varying in amount, being most evident in the rabbit killed with meningococcus. The preparations made for the express purpose of staining fibrin show these emboli most clearly even under the low power though they are

evident in the haemotoxylin stained preparation. Of these emboli a certain number become detached as may be seen in some of the pulmonary veins, they are then transmitted to the left ventricle (see typhoid rabbit) and thence may be carried to the various organs, *e.g.* kidney, liver, suprarenal. The fibrinous emboli are in many cases associated with cells and it is legitimate to suppose that by the injection of such massive doses of bacteria and their endo-toxins into the venous system some inflammation in this and in the branches of the pulmonary artery is produced sufficient to induce thrombosis.

All the animals underwent the same treatment, died with the same symptoms and their organs show an identical morbid anatomy. Two views may be put forward as to the cause of death: first that it is due to multiple capillary pulmonary embolism, and secondly that it is due to the toxic effects of the substances injected. When we consider however that one organism (*Sarcina lutea*) is not usually pathogenic at all, and that none are normally pathogenic to the rabbit, one is forced to the conclusion that the cause of death is the cause which can be readily demonstrated by the microscope, namely multiple capillary embolism of the lungs and secondarily of other organs.