FATAL ANAPHYLAXIS

FOLLOWING THE PROPHYLACTIC ADMINISTRATION OF ANTITETANIC SERUM.

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THAT the parenteral introduction of foreign protein in the form of antisera is not infrequently accompanied by more or less important constitutional and local manifestations of irritation or intoxication is generally appreciated. Fortunately, such symptoms consist, as a rule, simply in the development, a few (2 to 14) days after the injection, of urticarial and erythematous eruptions, and joint or muscle pains, accompanied sometimes by a certain degree of pyrexia. The patient is often very unhappy, but otherwise such examples of serum sickness are not of sufficient importance to contra-indicate the employment of sera for either prophylactic or therapeutic purposes.

From time to time, during the past 15 years, cases of severe and fatal reaction following the administration of horse serum have been recorded. The great majority of these cases have occurred among patients receiving the serum in the treatment of their infections. In the prophylactic injection of antitoxin-containing sera—e.g., antidiphtheritic and antitetanic sera—the amount of protein introduced is relatively very small and the material is commonly injected into the subcutaneous tissues. In consequence very few serious accidents have occurred.

Report of Case.

The case reported in this paper proves the possibility of a fatal reaction to the administration of horse serum in small doses. This case is reported, not as an objection to the routine injection of all wounded with antitetanic serum, but rather in order that a rare clinical accident may be placed upon record.

L./Sgt. E. was admitted to a casualty clearing station on Sept. 1st, 1916, at 10.15 A.M. A few hours previously he had received several small bomb wounds of both hands, the right thigh, and left calf. All wounds upon examination were found to be unimportant. The patient was in good general condition; he was a well-built man about 30 years of age. Pulse and temperature were normal.

As the patient had not received his antitetanic serum prior to admission, this was administered at 11.15 A.M. 750 units (U.S.A.) contained in 5 c.cm. of serum were injected subcutaneously over the right pectoralis major muscle. (There is the possibility that part of the serum was injected into the muscle.) The patient remained well until 1.30 P.M., two and a quarter hours after the serum inoculation, at which hour he commenced to vomit, and had a bloody diarrhoea. This gastro-intestinal disturbance was accompanied by a moderate degree of collapse. Between 1.30 and 5 P.M. he vomited eight times, and had six bowel movements. All bowel evacuations contained blood. The stools were watery, and contained small particles of faeces, and a moderate amount of small blood clot. The sister in charge of the case noted no blood in the vomitus.

Examination at 5 P.M. resulted in the following notes: "Pulse 104, temp. 102°8'F. Patient complains of moderate headache and thirst. There is slight generalised abdominal tenderness, no rigidity. The chest is negative, no complaint of respiratory distress, despite the fact that he is cyanosed and restless. The skin is 'goose-fleshed,' and covered with a mild erythema." From 5 P.M. to 11 P.M. the patient remained in this state of moderately severe collapse. He received water by mouth, otherwise no treatment was instituted, as his condition was not alarming.

At 11 P.M., after a slight vomiting attack, the collapsed state became very severe. He became pulseless at the radials, heart beat rose to 160–170. Extreme cyanosis supervened, and restlessness increased. During the night stimulation was pressed to the utmost. Pituitary extract, 1 c.cm. to the dose, was given every three hours. Strychnine, 1/30 gr., was given at 11 P.M., and continued in doses of 1/40 gr. every three hours. He received 3 pints of saline subcutaneously during the night, and oxygen almost continuously up to the time of death. Except for the fact that he became quieter and more comfortable while receiving oxygen, there was no response to stimulation.

At 6 A.M. on Sept. 2nd the following notes were made: "Pulse is absent at the wrist, heart-rate 180 and feeble. There is a very marked purplish discoloration (cyanotic erythema) of the whole body. This discoloration disappears upon pressure and returns very slowly. The extremities are cold. There has been no return of vomiting or diarrhoea."

Death ensued at 10.30 A.M., apparently due to cardiac failure secondary to drop in blood pressure. Respirations during the last three hours of life were at the rate of 48–54 per minute.

Note.—Patient stated that he had suffered during the past four or five years from periodic attacks of vomiting at three or four weeks' interval, always accompanied by bloody diarrhoea.

Autopsy.

Autopsy performed four hours post mortem; body is that of a well-developed, well-nourished man of, apparently about 30 years of age. Rigor mortis is moderate. Lividity is excessive, except over the centre of chest and abdomen. There is oedema of both pectoral regions (subcutaneous saline). Wounds are trivial.

Thymus is completely atrophied.

Thyroid is somewhat enlarged and contains a few minute cysts filled with colloid.

Peritoneal cavity: There is a normal amount of clear fluid, lymph nodes are larger than normal, those in the gastro-colic omentum are deep-red in colour. Appendix normal. Vessels (veins) of splanchnic area are moderately distended with fluid blood, especially those draining duodenum and the upper part of the jejunum.

Pleural cavities: Both cavities are obliterated by moderately dense adhesions.

Pericardial cavity: Negative.

Lungs: Owing to the pleural adhesions present the lungs were squeezed considerably in the process of removal. The lungs are, nevertheless, voluminous and downy, except over the posterior parts, which are boggy and dark in colour. The lungs are reddish-grey in colour and are covered over the whole surface with innumerable subpleural collections of deep purple-coloured blood. These patches vary in size from 1.5 to 5 mm. (Note: These hæmorrhagic patches are typical of those found in anaphylaxis in the guinea-pig.) Beneath the parietal pleura there is a smaller number of similar hæmorrhagic spots. The cut surface of the posterior parts exudes a considerable amount of bloody frothy fluid; the anterior portions show a dilatation of the alveoli and numerous small purplish-red spots.

Heart: Normal in size and shape. The right ventricle, especially, is filled with dark fluid blood and loose friable clot. Myocardium and endocardium are negative. Beneath the epicardium covering the auricles there are numerous small purplish spots measuring from 1 to 2.5 mm. in diameter.

Liver: Purplish in colour, normal in size and consistence. Cut surface exudes an increased amount of fluid blood. The gall-bladder is slightly distended.

Spleen: Weight about 150 g., exudes upon section a moderate amount of blood. The splenic vein is distended with fluid blood.

Pancreas: Negative, except for serous congestion.

Adrenals: Negative.

Kidneys: Congested.

Bladder: contains straw-coloured urine.

Stomach and intestine: The gut contains bile-stained fluid faeces. No blood is present. Solitary follicles are prominent. Peyer's patches are not enlarged. There is moderate superficial capillary engorgement in the stomach, particularly about both orifices.

Naked-eye diagnosis: "Anaphylactic lungs"; congestion of kidneys; chronic pleurisy; congestion of liver; multiple wounds (trivial); slight splanchnic dilatation.

Examination of heart's blood negative.

Microscopical Examination.

Examination of paraffin-embedded sections of heart, kidney, liver, mesenteric lymph nodes, and jejunum all negative but for a moderate to pronounced congestion of the small vessels, particularly in the liver, kidney, and lymph nodes.

Sections of the lung stained with hæmatoxylin and eosin and with fibrin stain reveal the following lesion. The general appearance of the sections is irregular. Different parts of the sections are composed of varying abnormalities of alveolar arrangement. In places the alveoli are compressed, their lumina being almost obliterated; in others they are greatly distended, with apparently a rupture of their walls, with the result that large irregular cavities are present. Some of the sections are composed chiefly of masses of blood clot, in which are included numerous large and small vacuoles (air bubbles). With the high power of the microscope these areas are found to represent places in which the normal alveolar arrangement is disorganised, the alveolar walls ruptured, and the resulting irregular cavities filled with red blood cells, fibrin, and serum. The arteries of the lung are normal in size and contain red blood cells; the veins are moderately distended with blood. The bronchioles are apparently contracted and many contain large numbers of red blood cells.

Discussion.

In so far as we are able to discover, the patient had not been previously wounded, nor had he received at any other time injections of horse serum. That he was an individual presenting a natural hypersensitiveness to horse serum is therefore a fair assumption. The fact that the same person is not infrequently sensitive to more than one foreign protein in all probability offers an explanation of the patient's history of repeated attacks of vomiting and bloody diarrhoea.

The foregoing case-report is that of a healthy man who collapsed following the hypodermic administration of a relatively small dose—5 c.cm.—of horse serum, and who died with symptoms during life identical with those which occur in anaphylactic shock in the dog, and with autopsy findings typical of those which are found in the guinea-pig. That the characteristic purplish congestion of the splanchnic area which is found at autopsy in dogs dying of anaphylactic shock was not more marked in our case is explained as being the result of the continuous stimulation employed in our effort to save the life of the patient.

That symptoms of respiratory spasm were not noted clinically is explained in part by the fact that, owing to pressure of work, the patient was not under constant supervision, and, more particularly, because the splanchnic reaction was predominant and so weakened the patient that expiratory dyspnoea was not sufficiently evident to be noted by the sister in charge of the case. Deficient oxygenation of the tissues during life was evidenced by the extreme degree of cyanosis.

It is now definitely established that man reacts to anaphylactic shock in one or other or both of two ways, in addition to the well-known cutaneous phenomena. Either he reacts in the manner which characterises the phenomenon in the dog—i.e., splanchnic dilatation, drop in blood pressure, cardiac failure, and death—or in the way in which the typical reaction occurs in the guinea-pig—i.e., bronchiole spasm, expiratory dyspnoea, and death from arrest of respiration.

OXYGEN AND AIR REPLACEMENT OF FLUID IN THE PLEURAL CAVITY.

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THE apparent complexity of the apparatus commonly employed for oxygen replacement may be the explanation of its infrequent performance. The following is a description of a simple method. All that is required is a Potain's aspirator or a home-made substitute for this, two bottles A and B, and an oxygen cylinder. The aspirator and bottles can easily be improvised. The method of making the latter is obvious, and the former can be made by using a bottle, similar to those figured but larger, with a Higginson's syringe fastened to the short tube, the action of which will give sufficient negative pressure.

One of the bottles (A) is fitted at (o) with a flexible rubber tube about 18 in. in length and a needle long enough to enter the pleural cavity, with a bore of 1 mm. to allow the easy escape of air. Morriston Davies's needle, made by Krohne and Seseman, is figured, as it is useful to have a tap, but an ordinary needle will do so long as the bore is of a sufficiently large diameter. The long tube is tapered slightly at (1). Bottle (B) is fitted at (3) with 2 or 3 in. of rubber tubing, which, when required, can be slipped on to the conical part of the long tube (1) of bottle A, and thus connect the two bottles. The long tube of this second bottle is also slightly tapered, so that a rubber tube from the oxygen cylinder can be pushed on with ease. Each long tube near the external opening can, after sterilising, be lightly packed with cotton-wool. The bottles are one-third filled with 1 in 20 carbolic acid solution.

To aspirate by means of automatic air replacement is very easy, and has been described in Halliday Sutherland's "Pulmonary Tuberculosis in General Practice."

The needle of the Potain's or home-made aspirator is inserted in the seventh or eighth interspace, just outside the line of the angle of the scapula, after first anæsthetising the track with novocaine. Complete local anæsthesia should always be assured. After withdrawing a certain quantity of the fluid—say, 10 oz.—insert the needle of bottle (A) into the interspace above, again using novocaine freely. At once, with certain exceptions which will be mentioned later, air will be drawn through tube (1), bubble through the carbolic solution, and enter the pleural cavity.

Aspiration is now continued until the chest is completely emptied, allowing the patient to recline more and more as the fluid decreases, so that at last the aspirating needle is in the most dependent part of the pleural cavity. So long as aspiration is continued air will steadily flow into the pleural cavity bubbling pretty regularly through the bottle. When all the fluid has been aspirated a bubbling hissing noise will indicate that air only is being withdrawn, and the operation can cease. It is well to leave a slight negative pressure; a little of the air, therefore, is aspirated, but not enough to produce the slightest discomfort to the patient. The needles are then withdrawn.

For oxygen replacement fill both bottles (A and B) with oxygen from the cylinder. Any type of cylinder will do. Commence aspirating as before, insert needle of bottle (A) and note the rate at which bubbles of air pass through the carbolic solution and the size of them. Now turn on the oxygen cylinder which is attached to bottle (B) and let the gas bubble through at the same rate that air is bubbling through (A). This is easily determined in a few seconds. Now connect bottles (A) and (B) and continue aspirating. Pure oxygen will now be passing into the pleural cavity. To prevent the production of a positive pressure in the chest disconnect the two bottles from time to time and see if air