CONCENTRATED ANTIPNEUMOCOCCAL SERUM IN THE TREATMENT OF LOBAR PNEUMONIA

BY

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(With Special Plate)

The following case appears to be of exceptional interest, as it illustrates unusual features in the onset, treatment, and termination of primary lobar pneumonia.

Clinical History

A robust young man, aged 19, was admitted to hospital at midday with a clinical history of the onset, at 8 o'clock in the morning, of sudden severe abdominal pain, chiefly in the left upper quadrant. He had nausea, but no vomiting; the bowels had acted that morning. There was no history of dyspepsia or of any abdominal symptom, no rigor, and no cough.

The pain continued, and was of such an agonizing character that the patient was immobilized and almost speechless. His face was drawn and livid, pulse 110, respirations 24, temperature 97° F. The abdomen was as rigid as a board, and extremely tender. The liver dullness was normal; no urine was available; rectal examination was negative; there were no physical signs in the lungs.

Under general anaesthesia (gas, oxygen, and ether) the abdomen was opened from the costal margin to the umbilicus by a right paramedian incision. A careful examination was made, of the stomach in particular, but nothing abnormal was found. The abdomen was closed without drainage.

The possibility of acute lobar pneumonia remained to be considered, and events soon confirmed a tentative diagnosis of this disease, for the temperature began to rise, and by evening a pleural friction was detected in the right axilla.

The picture of lobar pneumonia had become clear by the following day, there being widespread pleural friction and impairment of percussion note on the left side, and that evening, thirty-two hours from the onset of his illness, the patient expectorated a fleck of dark, heavily blood-stained sputum. The second day passed with every symptom of a lobar pneumonia of increasing severity, the pulse rate at night reaching 180 per minute. Forty-eight hours from the onset of the illness a radiograph of the chest was taken (Fig. 1, Special Plate), and the report was as follows:

Heart and trachea: not displaced. Right lung field: the upper zone is clear. There is an opacity in the mid zone, and in the lower zone an extension downwards towards the diaphragm of the hilar shadows. Left lung field shows a uniform opacity from apex to base, which is slightly clearer in the upper zone than towards the base. The appearances are consistent with a pneumonia of the left base, with either consolidation or thickened pleura above this. There is also an inflammatory lesion of the right mid and lower zones, which is either resolving or has not yet reached the stage of complete consolidation.

Examination of the sputum, which was now copious, fluid, and deeply blood-stained, showed large numbers of pneumococci. Type was determined in four hours by the rapid method described in the *Journal* of February 7th (p. 214),¹ and 20 c.cm. of the corresponding Type I concentrated antipneumococcal serum (Wellcome) was immediately administered intravenously, sixty hours from the onset of symptoms.

The patient was now desperately ill, and all the classical signs of consolidation of the left lung were present. The patch of pleurisy in the right axilla persisted, with accompanying bronchitis. The heart was normal in size and position. There was a well-marked albuminuria. No immediate shock accompanied the serum injection, but a rigor followed within an hour, as depicted on the Chart.

Twelve hours later, in the morning, cyanosis and distress were less evident, the mental state was clearer, and the toxæmia obviously reduced. There was undoubted improvement. A further intravenous dose of 20 c.cm. of concen-

trated serum was administered, and this dose was repeated twelve hours later. Whereas a vigorous rigor without sweating had followed the morning dose, the evening administration caused little disturbance, but was followed by profuse perspiration. Progressive improvement was noted throughout this, the third day, in the mental state, in cyanosis, and in the character and frequency of the respiration. The tongue became moist and cleaner. The only adverse feature was a persistent tachycardia, rate 160, uninfluenced by full doses of digitaline during three days. In other respects the pulse was of good quality. The fourth dose of 20 c.cm. of serum was given ninety-six hours after the onset. The patient had so far improved as to demand solid food; the tongue was clean.

Careful examination of the chest left no doubt in our minds that the left lung was consolidated; typical impairment on percussion and loud bronchial breathing were present, as before, on the left; the physical signs on the right were likewise unchanged. The heart was normal in position and size, but tachycardia still persisted; it seemed permissible to attribute this frequency in part to apprehension, for the patient was much concerned about his illness. The urine was now free from albumin. At 6 p.m. the pneumonia appeared to have abated further, and the patient was drowsy and comfortable. A final dose of 10 c.cm. of serum was given, making a total of 90 c.cm. Later in the same evening, however, he became restless, and the house-surgeon, on examining the chest, found an entire absence of breath sounds over the left lung, with gastric resonance rising in front to the level of the fourth rib. The patient vomited a black fluid, and his restlessness increased. He collapsed, and suddenly died, apparently of heart failure, at 4 a.m., 114 hours from the onset of the illness.

Post-mortem Findings

A partial necropsy was performed through the abdominal wound. Except for some plastic fibrin covering the peritoneal surface of the incision—clearly reparative—the wound and peritoneal cavity were healthy. The stomach was enormously dilated, and was filled with a thin, brown-black fluid; it was thrusting up the left cupola of the diaphragm so as to encroach on the left pleural cavity. When the diaphragm was opened the left lung was found almost entirely covered by a layer of soft yellow fibrin, a quarter of an inch in thickness, by which the parietal and visceral pleurae were loosely connected, the pleural surface of the left cupola of the diaphragm being especially involved in this process. The lung was completely collapsed, flabby, and airless. On section, the cut surface was dry; there was no evidence of consolidation or of bronchitis. The fibrin envelope was loosely adherent, and easily peeled off the surface of the lung. The condition is shown in Fig. 2 (Special Plate); the fibrin shell has been stripped to show the wrinkled surface of the collapsed lung. The right lung, by comparison, was voluminous, and appeared larger than a normal lung, the upper part being emphysematous. Small slate-grey areas of collapse were present only at the base. On section some congestion, but no consolidation, was found; the patch of pleurisy identified during life was confirmed. The heart appeared normal in every respect, chambers not dilated, muscle firm; no pericarditis.

Microscopic Appearances

Sections of the lung, studied under the microscope, confirmed the gross appearances. There was general congestion of the vascular system, and here and there red cells had

extravasated from congested or ruptured capillaries into the alveolar lumina. At the periphery of the lung the alveoli were collapsed, and contained a few desquamated epithelial cells. At the hilum the alveoli, although not distended, contained serum, alveolar epithelial cells, and a few polymorphocytes; pneumococci were clearly seen in some of these alveoli and in places in the perivascular lymphatics. Some alveoli were crowded with polymorphs; fibrin was absent. The epithelium of most of the bronchioles was completely desquamated, but the bronchi contained little secretion, thus confirming the macroscopical appearance of the dry cut surface of the lung and differing in this respect from the picture of a lobar pneumonia as commonly observed at necropsy on the fifth day of the disease. The microscopical appearances were practically those found when resolution of a pneumonic exudate is approaching completion, except that reparative changes in the bronchiolar epithelium were not yet apparent.²

The Blood Picture

A blood count on the morning of the third day of the illness showed 3,900 leucocytes per c.mm. and, later in the same day, before administration of serum, 6,000 per c.mm. On the morning of the fourth day the count was 9,000 per c.mm., and of the fifth 11,400 cells per c.mm., in each case before serum was given. The low cell count indicates a severe type of disease and failure of response on the part of the patient. The observed rise in the leucocyte count may be taken to indicate improvement. A sample of blood was collected post mortem, the serum separated, and the protective power estimated by mouse test. The patient's own pneumococcus was used; this was of maximum virulence, one ten-millionth of a cubic centimetre of a sixteen hours' blood-broth culture proving fatal to mice in forty hours. It is significant that the Type I antibody content of this serum was considerable, one-fifth of a cubic centimetre actually protecting mice against one thousand minimal lethal doses. The presence of so large a surplus of free antibody at this stage of pneumonia is, in our experience, clear evidence that the primary infective process has been overcome.

DISCUSSION

Gastric atony is a recognized complication both of lobar pneumonia and of acute abdominal disease and operation. Paresis, or even paralysis of the diaphragm, is apt to follow diaphragmatic pleurisy. Any or all of these factors may have contributed to the collapse of the lung. That the abdominal section had caused a severe disturbance of the autonomic nervous system was evident from the persistently rapid pulse uninfluenced by digitaline. The subsequent events are therefore easily understood.

The absence of consolidation of the left lung, which made complete collapse possible on the fifth day of the illness, is explicable on one hypothesis only—namely, that the antipneumococcal serum had entirely changed the normal sequence of intrapulmonary events. A state of fluid serous exudate into the pulmonary alveoli, characteristic of the second or third day of lobar pneumonia, must largely have persisted, instead of the comparatively static condition of solid hepatization proper to the fifth day. It seems probable that absorption of this fluid exudate must have been in rapid progress, and that the collapse of the lung, occurring over the period of about eight hours which preceded death, accelerated the expulsion of the inflammatory products.

Meanwhile, this remarkable case appears to us to afford unassailable evidence in favour of the use of concentrated antipneumococcal serum early in pneumonia. Had it not been for the unfortunate and purely accidental collapse of the lung, we are confident that our patient would have made a good recovery.

SUMMARY

The salient features of this case are as follows:

1. The onset exactly simulated an acute abdominal emergency.

2. The course of the case (excluding the unavoidable accident which caused death) illustrates the type of response to be anticipated from serum treatment of primary lobar pneumonia, due to the pneumococcal Types I and II, when exhibited early in the disease.

3. The pathological changes which successively follow in lobar pneumonia appear to have been profoundly modified by serum treatment, so that the normal process of inflammation has been curtailed and the disease process aborted.

4. The radiographic evidence and the careful study of physical signs prove beyond doubt that the lung was at one stage the seat of what is described as pneumonic consolidation. The findings post mortem show that the resolution of this process was almost complete by the fifth day of disease.

The observations recorded form part of an inquiry into the serum treatment of pneumonia undertaken by us for the Medical Research Council.

REFERENCES

- ¹ Armstrong, R. R.: *British Medical Journal*, 1931, i, 214.
- ² Armstrong and Gaskell: *Journ. Path. and Bact.*, 1921, xxiv, 369.

THE MODERN CONCEPTION OF EARLY PHTHISIS*

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(With Special Plate)

In order that I may make clear the new teaching, I shall first give a short summary of the old doctrine on this subject, which was that phthisis developed from a small discrete lesion situated just below the apex of the lung. The ulcer might heal to form an apical scar, or, on the other hand, might slowly progress to involve the surrounding lung tissue, and thus gradually spread the disease from apex to base. This orthodox view had its foundation among the pathologists, who, in thousands of necropsies on cases of pulmonary tuberculosis, found the oldest lesion in the apical region, with less intense involvement of the lower parts of the lung; further, they discovered an apical scar in 95 per cent. of patients who had not died from pulmonary tuberculosis. They therefore argued that in those cases in which pulmonary tuberculosis developed it most probably had its origin in the apical region, from which it spread downwards. The clinical interpretation placed on this teaching was that the first signs of pulmonary tuberculosis were usually found in the apical region, that the disease was of slow, insidious onset, and that it spread from apex to base. Further constitutional symptoms (pyrexia, anorexia, loss of weight, and lassitude) were often shown some considerable time before the disease process gave rise to physical signs in the chest. Therefore, in the diagnosis of the early case of phthisis, great stress was laid on the history of constitutional symptoms, and physical examination was concentrated on the apical regions. Doubts were first cast on this old teaching by statistical evidence when it was established in Germany that, in 1,438 cases¹ in which this apical lesion was diagnosed, only 7 per cent. developed phthisis; yet the death rate from this disease among the general population was 10 per cent. In other words, patients who were regarded as early cases of the disease did not develop the disease with any greater

* An address delivered to the general practitioners of Bermondsey.

H. A. HARRIS: LINES OF ARRESTED GROWTH IN THE LONG BONES OF DIABETIC CHILDREN

FIG. 1.—Radiogram of the knee of a diabetic girl of 13, showing multiple lines of arrested growth in the metaphysis of the femur and tibia.

FIG. 2.—Radiogram of the tibia of a diabetic girl of 12, showing lines of arrested growth in the bone.

R. S. JOHNSON AND R. R. ARMSTRONG: PNEUMONIA TREATED BY CONCENTRATED ANTIPNEUMOCOCCAL SERUM

FIG. 1.—Radiogram of chest showing pneumonia of left base and also an inflammatory lesion of the right mid and lower zones.

FIG. 2.—Specimen of left lung, collapsed and empty on the fifth day of disease. The fibrin envelope has been partly stripped to show the wrinkled surface of the lung.