CHANGES IN HAEMOGLOBIN CONCENTRATION IN THE ACUTE STAGE OF LOBAR PNEUMONIA

BY

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The frequent occurrence of delayed resolution in lobar pneumonia treated with sulphonamides has emphasized the need for the investigation of factors which might lead to further elucidation of the process of resolution. Ross (1945) demonstrated that those patients who subsequently developed delayed resolution had, on admission to hospital, a lower concentration of plasma protein than those whose consolidation resolved within the normal time. Although it seemed possible that such low plasma proteins might be due to a dietetic deficiency in protein, she also suggested that the onset of pneumonia might itself cause a fall in the plasma protein content. It seemed reasonable to argue that, if a loss of plasma protein were initiated by the disease process, the presence of "oligaemic shock," with accompanying haemoconcentration, might be a factor in the severe case of pneumonia and might retard the process of resolution. It was therefore decided to repeat Ross's experiment, with the addition of a careful study of the course of the haemoglobin concentration.

Methods

The investigation was carried out concurrently with, and upon the same subjects as, an experiment comparing the respective therapeutic effect of sulphonamides and penicillin on the course of lobar pneumonia (Anderson and Ferguson, 1945). The patients were men of 35 years or more. They received either sulphonamide or penicillin therapy. Already it has been recorded that the results of treatment were similar. Further, as a careful comparison of the haemoglobin changes in the two groups showed no difference between them, they have been regarded for the purposes of the present investigation as a single series.

Heparinized venous blood, withdrawn from a superficial vein without stasis, was used for all haemoglobin and plasma protein estimations. Plasma protein concentrations were estimated only on the blood sample obtained upon the patient's admission to hospital. The estimations were made by the refractometric method.

A photo-electric absorptiometer of the "Spekker" type was used to estimate haemoglobin concentration. Haemoglobin was converted to oxyhaemoglobin by blowing an accurately measured 0.1 ml. of heparinized blood into 10 ml. of a 0.4% solution of ammonia in distilled water. The readings obtained on the "Spekker" were converted to absolute values by means of a graph. This graph had been obtained previously by plotting serial dilutions of a blood of known oxygen capacity against their corresponding logarithmic values.

Each patient's haemoglobin concentration was estimated on admission and, if possible, for the four succeeding days. Thereafter, unless clinical findings indicated that more frequent investigation might be of interest, haemoglobin estimations were repeated only at weekly intervals. The majority of estimations were duplicated, and a difference greater than 0.2 g. was considered to be inaccurate.

Results of Investigation

(a) *Admission Plasma Protein Concentration.*—The admission plasma protein concentrations were estimated on 84 patients whose recovery was uncomplicated either by

empyema or by sterile effusion. These cases were divided into two groups:

Group A contained those patients in whom, by the 28th day of illness, there remained no clinical or radiological evidence of a pneumonic consolidation. Such patients were considered to have shown "normal resolution."

Group B contained all those patients in whom the pneumonic consolidation persisted beyond 28 days. Such patients were considered to have "delayed resolution."

The percentage frequency distribution of the plasma protein concentration in these two groups is shown in Fig. 1 and Table I. It is apparent that the majority of Group B

FIG. 1.—Admission total plasma protein level.

TABLE I.—Admission Total Plasma Protein Level (Actual Figures)

	Protein Level in G. %					Total No. of Cases
	4.1-5	5.1-6	6.1-7	7.1-8	8.1-9	
Cases resolving in 28 days	2	3	13	18	4	40
	5%	7.5%	32.5%	45%	10%	100%
Cases resolving after 28 days	2	8	20	12	2	44
	4.5%	18.2%	45.5%	27.3%	4.5%	100%

cases on admission to hospital have a lower concentration of plasma proteins than have Group A cases, for in 55% of Group A cases a plasma protein concentration of between 7.1 and 9.0 g. % was obtained, whereas only 31.8% of Group B cases attained this level. These figures confirm Ross's observation except that in the present series the differences are less marked. It may be noted that Ross's cases included all male patients from 20 years of age upwards, whereas the present series contains only patients over 35 years. Since this selection concentrates attention on the age group in which the disease is most severe it would be natural for the difference to be less obvious.

(b) *Admission Haemoglobin Concentration.*—The distribution of admission haemoglobin concentration in all

TABLE II.—Correlation Between Admission, Haemoglobin Concentration, Duration of Illness, and Subsequent Time of Resolution

	Hb Concentration (G. %)						% of Cases showing		Total No. of Cases
	19-17	17-15	15-13	13-11	11-9	Aver.	Normal Resol.	Delayed Resol.	
All cases on admission	1	15	53	38	4	13.48			111
Cases admitted on 1st to 3rd day of illness	1	7	35	18	1	13.65	61.4	38.6	62
Cases admitted on 4th day of illness and over	—	8	18	20	3	13.26	33.3	66.7	49
Cases with Grade I consolidation	—	6	10	7	—	13.91	86	14	23
Cases with Grade II consolidation	1	5	22	17	—	13.56	41	59	45
Cases with Grade III consolidation	—	3	18	14	4	13.03	15	85	39

patients was grouped according to the duration of illness and density of consolidation. The frequency of delayed resolution in each group was also recorded (Table II). Study of this table suggests that cases admitted early in their illness tend to have an average admission haemoglobin concentration slightly higher than those admitted late and that delayed resolution is rather more common in the latter group. In an attempt to obtain some standard which might reflect the haemoglobin level before admission, nine healthy male relatives of the same age group were selected, since, living under the same conditions as the patients, they might

be expected to show a similar blood picture. The average haemoglobin concentration of these controls was 14.98 g. %, a level within normal limits, and one which is in accord with that reported by Marshall (1946)—14.6 g. per cent. for male blood donors of this age group in Glasgow. A comparison of this figure with the average admission haemoglobin in pneumonic patients reveals that the latter is 1.5 g. lower than the control figure. These figures suggested that the haemoglobin concentration was lowered by the onset of pneumonia and that as the duration of the illness increased the level might be further reduced.

It seemed possible that the effect of a longer duration of the disease might be to increase the extent of consolidation. If such were the case, then a correlation between the haemoglobin level present on admission to hospital and the density of consolidation as assessed from a radiograph might be expected. To test this, three arbitrary grades of radiographic density were chosen. These were defined as follows:

Grade I Consolidation.—Those cases in which the lung markings could be seen clearly through the consolidation were allocated to this section.

Grade II Consolidation.—Into this group were placed cases in which the lung markings could still be discerned through the consolidation, but much less clearly than in Grade I.

Grade III Consolidation.—Into this group were placed those in which the consolidation was so dense that no lung markings were apparent.

When a comparison is made of the admission haemoglobin values in these three groups (Table II) we find a slight trend downwards in the haemoglobin concentration as the density of the consolidation increases. As one might expect, there is a direct correlation between the density of the original consolidation and the speed of resolution. This is shown very clearly in that 85% of those patients with the densest consolidation (Grade III) developed delayed resolution, where-

as among those patients with the least dense consolidation (Grade I) only 14% showed this abnormality. Of more importance, however, the findings give no support to Ross's contention that "shock" might account for the low plasma protein levels in pneumonia, since the consequent haemoconcentration which should be present was not found.

Mean Daily Haemoglobin Levels during Course of Pneumonia

Since it appeared that haemoglobin concentration might be affected by the duration of illness prior to admission to hospital the

FIG. 2

mean haemoglobin levels for each day of illness were calculated. The results of this analysis are depicted in Fig. 2, A. It is evident that in pneumonia, during the first 12 days of illness there is a progressive fall in haemoglobin concentration which follows a steady curvilinear course. Further, a tentative suggestion may be made that, as the original haemoglobin concentration of the pneumonic patient was probably similar to that of his male relatives, a fall in haemoglobin value had already occurred before his admission to hospital.

When a comparison of the average daily haemoglobin values was made between patients whose consolidation resolved normally and those in whom resolution was delayed, the graphs shown in Fig. 2, B were obtained. It can be seen that the curve for those patients who developed

delayed resolution shows a tendency to follow a rather lower level than that found in patients whose consolidation resolved within a normal period. It was now becoming manifest that haemoconcentration was not normally found in cases of pneumonia. Indeed, the haemoglobin value appeared to fall progressively below normal limits during the fastigium of the disease; this fall was most marked in cases which subsequently developed delayed resolution.

Discussion

The initiation of the pneumonic process must occasion a loss of plasma into the affected lung. It seems reasonable to assume that this depletion will be proportionate to the volume of lung affected. Loss of protein from the plasma would naturally cause a mechanical haemodilution, although in a normal healthy subject one would expect such a change to be transitory and a rapid return of plasma protein and haemoglobin to normal levels to occur within two or three days. Yet in pneumonia the haemoglobin concentration continued to fall.

Such a rapid fall in haemoglobin concentration does not seem to be in keeping with the onset of a simple hypochromic anaemia produced by a sudden cessation of iron absorption. A continuous loss of blood by haemolysis might easily produce such a result, but examination of the blood of six patients during the first five days showed no evidence of reticulocytosis. It seemed most likely, therefore, that the fall in haemoglobin concentration was caused by haemodilution, and, indeed, Rutstein and his co-workers (1945) have shown that in the acute stage of lobar pneumonia an increase does occur in both the plasma volume and the volume of the extracellular fluid.

Seaman and Ponder (1943) obtained rather similar findings in post-operative cases and showed that after operation the fall in haemoglobin concentration was greater than could be expected from the volume of blood lost. Findings so similar in two entirely different conditions might suggest that, in each, the phenomenon may be a response to injury. It may be that the injury to tissue, no matter what the assaulting mechanism be, produces a depression of the haemopoietic system.

Madden and Whipple (1940) express the view that the liver produces all albumin and much of the globulin required by the body, and observe that there is some evidence to show that, in dogs, infection can limit protein formation. If the haemopoietic system were thus depressed the liver might not only be unable to restore the plasma protein lost initially into the lung, but also might be inadequate in replacing the normal physiological daily loss. A similar continuous decrease in the number of circulating erythrocytes might also result. Such a loss of plasma protein might be expected to produce a fall in osmotic pressure and a resulting decrease in plasma volume, with marked peripheral failure. Yet in pneumonia there is an increase in plasma volume.

It is interesting that in nephrosis, despite a very low plasma protein concentration, a normal or almost normal plasma volume is found. Warren, Merrill, and Stead (1943) have suggested that the presence of an increased extracellular fluid volume may be the mechanism whereby the plasma volume is maintained in this disease. In experiments on dogs these workers have demonstrated that when the extracellular fluid was increased by continuous infusion until oedema occurred a normal plasma volume could be maintained despite a continuous loss of plasma protein.

It seems possible that, in pneumonia, retention of orally administered fluid produces a similar phenomenon and

that the extravascular fluid and plasma volume remain increased until such time as the factor which inhibits the production of new plasma protein and fresh erythrocytes is overcome.

These findings might be linked with the lowered blood chloride levels and chloride retention found in pneumonic patients. If an excessive quantity of vascular and extravascular fluid were present then it would not be surprising that a concurrent retention of chlorides should occur and that, despite this, the chloride concentration in the blood should be low.

It would thus appear that low plasma protein and low haemoglobin levels found in pneumonia are not in themselves causative factors in delaying the speed of resolution, but that these findings indicate an extensive and dense consolidation which is itself a prime factor in the speed with which resolution is concluded. There would seem to be need for further study of the biological changes to which the onset of an infective process gives rise.

Summary

The haemoglobin concentration of patients suffering from pneumonia was studied by repeated examination over a period covering the acute stage of the disease. There was no evidence of haemoconcentration. The haemoglobin concentration fell progressively during the first 12 days in hospital. It is suggested that this reflects a haemodilution found most markedly in the severe case.

The presence of low plasma protein concentration and low haemoglobin in cases of pneumonia does not cause delayed resolution, but merely parallels the density of the consolidation, which is itself important in deciding the time of resolution.

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REFERENCES

- Anderson, T., and Ferguson, M. S. (1945). *Lancet*, **2**, 805.
Madden, S. C., and Whipple, G. H. (1940). *Physiol. Rev.*, **20**, 194.
Marshall, A. J. (1946). *Glasg. med. J., n.s.*, **27**, 1.
Ross, C. A. C. (1945). *Ibid.*, **143**, 59.
Rutstein, D. D., Thomson, K. J., Tolmach, D. M., Walker, W. H., and Floody, R. J. (1945). *J. clin. Invest.*, **24**, 11.
Seaman, B. W., and Ponder, E. (1943). *Ibid.*, **22**, 673.
Warren, J. V., Merrill, A. J., and Stead, E. A. (1943). *Ibid.*, **22**, 635.

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