CHLORIDE METABOLISM IN PNEUMONIA AND ACUTE FEVERS.¹

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PART I.—CLINICAL.

Historical.—Diminution of the chlorides in the urine in cases of pneumonia was discovered by Redtenbacher (¹) in 1850. The discovery was made incidentally, in the course of an investigation into the relation between the amount of inorganic salts in the urine and its specific gravity. He investigated in all nearly eighty cases, and came to the conclusion that "the chlorine compounds in the urine in inflammation of the lungs are in direct proportion to the increase and decrease of the inflammation itself." His observations seem to have attracted considerable attention, and in the year 1852 we find an important paper on the subject by L. S. Beale (²). I shall have occasion to refer in detail to this paper at a later period, but may state here that Beale concluded that "in pneumonia there is a total absence of sodium chloride in the urine at or about the period of hepatisation," and that soon after resolution it is restored, often in considerable quantity. In 1869, in a paper by Unruh (³), tables are given showing the course of the chloride excretion in pneumonia, but without adding much to our knowledge. Fränkel, in the *Charité Annalen* for 1875, deals with the post-critical output of urea, and incidentally records some observations on the chlorides. I shall have occasion to consider his observations when dealing with the post-critical chloride excretion. Röhmann (⁴), in a paper published in 1880, was the first to prove that the diminished excretion of chlorides in pneumonia is really due to the temporary retention of these salts within the body. The most recent contribution to the clinical side of the subject has been from Terray (⁵), who investigated the chloride excretion in five cases of pneumonia, of one of which he gives a detailed table. Excluding the observations of Redtenbacher, which

¹ The research, the results of which are contained in this paper, was carried out during the writer's tenure of the Leckie-Mactier Fellowship, University of Edinburgh. The clinical observations were made in the wards of the Royal Infirmary, Edinburgh. The analytical and other work was carried out partly in the Physiological Laboratory, University of Edinburgh, and partly at the London Hospital Medical College.

were mainly qualitative, the cases detailed by the above writers do not amount to much more than a dozen in all. In some points their statements are not in harmony, but from their collective results the following facts emerge:—(1) The chloride output during an attack of pneumonia is greatly diminished; (2) this diminution is due to the retention of these salts within the body; (3) after the crisis there is often an excessive excretion. The points which require further elucidation by clinical observation are these:—(1) The degree of diminution in the excretion of chlorides. As to this, the statements of previous writers are very conflicting, some asserting that in all cases of pneumonia the urinary chlorides quite disappear, while others maintain that these are never, under any circumstances, altogether absent. (2) The relation between the diminution of chlorides and the amount of fever present. As many of the original observations were made before the days of the clinical thermometer, this point still requires clearing up. (3) The influence upon the chloride diminution of the extent of lung involved. Very little reference is made to this in the literature, and yet it is a point which has important bearings both on the diagnostic value of the chloride diminution and on the theories which have been advanced to explain its occurrence. (4) The association between the presence or absence of chlorides and that of albuminuria in cases of pneumonia. This also has important bearings on the discussion of the reason for the disappearance of the chlorides. The attention of the writer was specially directed to these points during the clinical part of this investigation. The facts upon which his conclusions are based include the results of daily quantitative estimations of the chlorides in twelve cases of pneumonia throughout the course of the fever, and, in some cases, for some time into convalescence. Qualitative observations were also made in a much larger number of cases. A selection of these cases will be found in the protocols at the end of this paper, and in most of them the results have been represented both in a tabular and graphic form. I shall discuss these results under the heads already mentioned—

1. *Amount of diminution.*—The results of my observations on this point show that a *total* disappearance of the urinary chlorides does occur in pneumonia, but not in all cases. Of the eight cases of which protocols are given, chlorides were entirely absent at some period in three. By entirely absent one means that on the addition of nitrate of silver and nitric acid to a sample, not a trace of a precipitate appeared. In four of the cases, at the time of maximum reduction, a trace was still present, *i.e.* an amount which, though appreciable, could not be accurately estimated. In only one case was there a considerable amount of chloride present throughout the disease. From qualitative observations also on a number of other cases, I can confirm the statement of Redtenbacher and Beale that total absence of chlorides does sometimes occur for a longer or shorter

period during the course of a pneumonia. The total absence may last only for a few days or even one day; occasionally, it persists throughout the whole length of the attack (Case 5). If total absence falls on one day only, that is not necessarily at the height of the disease. In the majority of cases the chlorides are diminished to such an extent that mere traces are present for at least one or two days. Rarely does the average excretion, throughout the attack, exceed 2 grms. of sodium chloride daily.

2. *Relation of chloride diminution to height of fever.*—A glance at the appended charts, which show the curves of temperature and chloride excreted in six cases, shows at once that there is no definite relation between the two. A case with a high temperature may have a considerable chloride output, while one in which the temperature is by no means high may be excreting none at all. Take, for example, Case 3. On the fourth day of the disease this patient had an average temperature of 102° F., and a total sodium chloride output of 2.04 grms. On the eighth day the temperature was the same, but the chlorides had risen to more than 6 grms., whilst the amount of salt in the food had only increased by 0.3 gm. In Case 6, again, we have a patient with a temperature of only 98° F., showing an entire absence of chlorides from the urine, whilst in Case 2 we find a patient with a temperature of 103° F. excreting 2 grms. daily. This absence of any connection between chloride output and the amount of fever is, perhaps, less surprising when one recollects that the height of the temperature is no criterion of the severity of a case of pneumonia.

3. It would seem that the *extent of lung involved* has also no necessary influence on the amount of chloride excreted. Here one has to rely mainly upon post-mortem evidence, owing to the difficulties of precisely mapping out the extent of the hepatised lung during life; but careful clinical observation also points to the same conclusion. As examples, take Cases 5 and 6. In the former of these the consolidation could be made out to be limited almost exactly to the middle lobe of the right lung; in the latter, physical signs could only be detected over an area about 2 square inches in extent; yet, in both, the chlorides were entirely wanting in the urine. On the other hand, one meets with cases of complete consolidation of one lung, in which a small amount of chloride remains persistently present in the urine. The absence of connection between degree of chloride diminution and amount of lung involved is further borne out by the fact, which the charts also exhibit, that there is not always a progressive diminution of chlorides as the inflammation spreads. On the contrary, the diminution is often greater in the early stages of the disease than it is later. I have not had the opportunity of observing a case from the very outset, but von Noorden cites one in which even in the first twenty-four hours the chloride excretion had fallen to 2.2 grms.

4. *Behaviour of other urinary constituents in pneumonia.*—Of these, urea has been most subjected to research. So thoroughly, indeed, has this part of the subject been dealt with, that I have not considered it necessary to make any fresh observations upon it, but shall merely refer to the results already published by others. It was found by Unruh that the urea excretion is increased in pneumonia as in other fevers, and also that the increased excretion persists for some days after the crisis. Indeed, there is often a considerable rise in the excretion, to be observed first at and immediately after the crisis. The later observations of Fränkel (⁶) confirm these results. It has more recently been shown by the careful observations of Wood and Marshall (⁷) that whilst urea is increased in fevers, there is no exact parallelism between the curve of the temperature and that of the urea output. The behaviour of the mineral constituents has been less studied. Fürbringer (⁸) has estimated the sulphates, and finds that they are increased to a greater extent in pneumonia than in any other fever. Neubauer and Vogel quote additional analyses bringing out the same fact, and the few observations which the writer has made fully agree with their conclusions.

The statements of different writers as to the behaviour of the phosphates are very conflicting. Von Jaksch¹ states that he has, unlike others, found phosphoric acid increased in some, though not all, cases of lobar pneumonia in children. Neubauer quotes Brattler, to the effect that there is an increased excretion in all acute febrile conditions. He himself gives figures which show in some cases an increase, in others a diminution, and adds, "in diseases of short duration, even although accompanied by much fever, the diminution of the phosphoric acid is at times scarcely perceptible." The detailed observations of my own cases will be found in the protocols, along with charts, but I may state here that the net result showed that phosphoric acid tends to be slightly increased during the fever, falling after the crisis, but occasionally showing a rise again about the third or fourth day of convalescence.

One may say, then, that the other typical urinary ingredients do not in the least behave in pneumonia as the chlorides do. They tend to be increased during the fever whilst the chlorides are diminished, the increase being usually absolute and not merely relative to diet. Marked diminution—much more total absence—is characteristic of the chlorides, and of them alone.

Albuminuria also shows no constant relation to chloride diminution. Absence or diminution of chlorides is the rule in pneumonia, whereas albuminuria only occurs in a certain percentage of cases. Thus Fränkel and Reiche (¹⁰) found albuminuria in twenty-four out of thirty-six fatal cases. Rosenstein (¹¹), in 130 cases examined, found albuminuria in only 23 per cent., and Crämer (¹²), in 45

¹ "Clinical Diagnosis."

per cent. of sixty-six cases. An examination of individual cases also shows the absence of any relation between the presence of albumin in the urine and the diminution of the chlorides. Thus, in some of my cases, entire absence of chlorides coincided with absence of albumin, whereas in others both chlorides and albumin were present together.

Post-critical excretion.—If we would understand the significance of the diminution of the chlorides during the febrile period of a pneumonia we must study their behaviour for some time after the crisis. This I have been able to do in several cases, and the results have been compared with the figures given in the tables of other writers (see Unruh, Fränkel, and Röhmann, already quoted). If the accompanying charts be examined it will be seen that the excretion continues very low—sometimes absent—for some time after the temperature has fallen (see especially Charts, 1, 2, 3, and 4). The crisis, therefore, is not immediately followed by an increase in the chlorides. It is not, as a rule, till about two days after the temperature has fallen that the chlorides reappear. This they sometimes do with the most striking suddenness. I have frequently seen the chlorides practically absent from the urine on one day, while on the day following they were present in an amount almost equal to the normal.

This sudden and excessive excretion may be called the epicritical excretion. It may reach the amount of the normal daily chloride excretion, or fall somewhat short of that, but is always in excess of the amount of chloride ingested in the corresponding period of time. It is comparable to the large excretion of urea which follows the crisis—the so-called epicritical urea excretion, which has been more studied. The two, however, are not coincident. In the tables given by Unruh and others it is seen that the epicritical nitrogen excretion usually follows immediately after the crisis, whereas, in the case of the chlorides, as we have seen, two days usually elapse before the excess appears. The significance of these epicritical excretions will be discussed later. At present I would only point out that, on reference to the charts, one can see that sometimes, though not always, the excessive excretion is followed by a temporary fall, which, in turn, is succeeded by a gradual rise till the normal is reached and maintained during convalescence.

Relation of output to intake of chlorides during the course of a pneumonia.—I have estimated the amount of chlorides in the food in four of the cases appended. The results are represented graphically in Charts 5, 6, and 7, and in tabular form only in Case 5. It will be observed that in all of them the amount of chloride ingested during the febrile period exceeded the amount excreted. In other words, as far as the urine at least is concerned, it would seem as if a retention of chlorides within the body took place. Further, it will be noticed, that this retention continues until the epicritical excretion

is reached, when the amount of chlorides in the urine surpasses (often, as in Case 7, very considerably) the amount in the food. In the only case (No. 3) in which the observations were continued far into convalescence, it is seen that the urinary chlorides again sank below the level of the quantity ingested, but soon rose again, till, in about ten days after the crisis, the intake and output were once more approximately equal. The second fall in chloride excretion observed in this case would probably be found to be of common occurrence, and is to be regarded as a compensation for the excessive excretion which follows the crisis in which the output of chlorides in the urine frequently more than makes up for the amount retained during the febrile period of the disease.

These observations are quite in harmony with those of Röhmann⁽⁴⁾ and Terray⁽⁵⁾—the only ones, so far as I am aware, previously published. Röhmann compared the intake and output of chlorides in three cases of pneumonia. He found that the ingestion during the febrile period exceeded the excretion by about 1 to 2 grms. daily. Terray only gives figures from one case. He also found a daily retention of about 2 grms. of sodium chloride during the fever period. Both observers found that after the crisis there is, for a longer or shorter time, an increased excretion, so that more chlorides were given out than are taken in. Terray also found in his case a secondary retention during convalescence such as I have shown to have occurred in Case 3.

Diagnostic value of the diminution of the urinary chlorides in pneumonia.—It must be admitted that this point has, to some extent, been lost sight of in recent years. A generation ago it seems to have been more considered. In most text-books of medicine, and even in those which deal specially with diagnosis, the diagnostic value of the behaviour of the urinary chlorides is hardly referred to. The tendency seems to be to regard their occasional disappearance rather as an interesting fact in chemical pathology than as being of any real service to the physician. In trying to arrive at sound conclusions in this matter I shall consider the disappearance of the chlorides as an aid in the diagnosis of pneumonia—(1) from other acute fevers, (2) from other pulmonary diseases.

1. It may be remarked, in the first place, that fever does not *per se* lead to any marked reduction of chlorides in the urine, if the restricted diet be taken into account. This is especially true of cases of chronic or prolonged fever. *Typhoid* belongs to this class, and accordingly one finds that it is only in the early stages of typhoid that any marked reduction of chlorides occurs. Table I., on p. 412, constructed from the observations of Moos and of Brattler,¹ shows the average chloride excretion per day in each week of the fever.

In Unruh's cases⁽³⁾, the average daily excretion is even higher—

¹ "Ein Beitrag Zur Urologie," S. 19.

amounting to nearly 5 grms. Terray⁽⁵⁾ gives daily analyses in one case. The average was 3 to 4 grms. per day. It is thus seen that the reduction of chlorides in typhoid is not marked, except during the first week, and even then is by no means at zero. In a doubtful case, therefore, a reduction of chlorides to anything like near the vanishing point would be against the diagnosis of enteric fever. Especially could this be the case, if diarrhoea were absent, for the existence of the latter may carry off a good deal of chloride by the intestine, and so lead to a diminution of the amount excreted by the kidney.

Howitz⁽²⁹⁾, indeed, asserts that he has been able to diagnose the supervention of pneumonia in the course of typhoid fever by a sudden diminution of the urinary chlorides.

TABLE I.

	Moos (Eighteen Cases).	BRATTLER (Ten Cases).
First week . . .	0·9 grms.	1·8 grms.
Second „ . . .	1·1 „	2·8 „
Third „ . . .	2·4 „	1·7 „
Fourth „ . . .	10·7 „	3·7 „
Fifth „ . . .	...	5·2 „

Typhus is a typically acute fever, and in it therefore one would expect to meet with a much more marked reduction of chlorides. This is found to be the case. Thus Murchison⁽¹³⁾ asserts that by the eighth day of a case of typhus, the chlorides have vanished to a mere trace, or may be entirely absent. Parkes⁽²¹⁾ makes a very similar statement. On the other hand, in the cases recorded by Unruh,¹ the daily average in one case amounted to 2·2 grms., while in two others it was more than 3 grms. Bennett⁽¹⁴⁾ also mentions a case where he was able to diagnose the supervention of pneumonia, in a patient who already had typhus, by the sudden fall in the excretion of chlorides. I have myself only had the opportunity of examining the urine in one case of typhus—in that the chlorides were reduced to a mere trace.

As regards the behaviour of the chlorides in *scarlatina* but few observations are on record. Brattler² states that they are sometimes greatly diminished. I have estimated the chlorides in six cases of scarlatina, at different periods of the disease, with the results shown in Table II.

I have since examined other two cases, neither of which was at

¹ *Op. cit.*² *Op. cit.*

the height of the fever, but both showing the presence of albumin in the urine. The chlorides were abundant in each case. Taking the cases as a whole, it is seen that the chlorides are not constantly reduced in scarlatina. In several of the cases, indeed, the quantity excreted exceeded that which was ingested in the corresponding period.

TABLE II.

Case.	Day.	Urine in C.c.	Total NaCl in Urine.	NaCl in Food (approxim.).	P ₂ O ₅ in Urine.	Temperature.
1	3rd	570	0·8	1·39	Almost absent.	101°-101°·6 F.
2	5th	560	0·8	1·59	0·341	103°-102° „
3	4th	825	2·39	1·1	1·32	102°·6-101° „
4	5th	968	4·0	1·59	0·96	101°·4-102° „
5	3rd	750	0·97	1·19	1·57	103°·6-104° „
6	(?)	909	5·7	3·40	...	103° „

In *acute rheumatism* the chlorides are sometimes greatly reduced during the febrile period. The exact extent of the diminution has varied considerably in the cases I have examined; but it must undoubtedly be classed with those diseases in which an almost complete disappearance of chlorides may sometimes be expected to occur.

I have had no opportunity of examining the urine in cases of *relapsing fever* or *smallpox*. In the former the chlorides are said to be considerably reduced (Unruh and others); as regards the latter, I can find no definite statement. Nor can I find any observations on the behaviour of the chlorides in an attack of quinsy.

In *malaria* the behaviour of the chlorides is altogether exceptional. Instead of being at all diminished, they are actually increased in amount during the febrile period. Observations on this point will be found in the papers of Röhmman, Terray, and others already quoted. The other solid ingredients are increased at the same time. This would appear to hold good for all varieties of malarial fever. The explanation of this anomaly must be deferred till later; but at present I would simply point out that the fact is worth bearing in mind, from a diagnostic point of view. In a doubtful case it might prove of considerable value.

To sum up, regarding the aid which diminution of the urinary chlorides affords in the diagnosis of pneumonia from other acute fevers, it is obvious that mere diminution is not pathognomonic of pneumonia. A case of high fever with the chlorides reduced to a mere trace might be one of typhus fever or of acute rheumatism, as well as a pneumonia. On the other hand, a case of high fever, which showed the presence of chlorides in the urine in fair abundance, is almost certainly *not* a case

of pneumonia. The test, therefore, is of negative rather than positive value. In the diagnosis of pneumonia from malaria, on the other hand, an investigation of the chlorides in the urine is of direct help, the excretion being diminished in the former disease, and increased, or at least abundant, in the latter.

2. In the diagnosis of croupous pneumonia from other pulmonary diseases, the estimation of the urinary chlorides is of even greater importance, croupous pneumonia being the only pulmonary condition associated with a constant and marked diminution of these salts. Thus in pleurisy, even with large effusion, there is not, as a rule, any appreciable diminution of chlorides. Even with the chest three-parts full of a recent effusion, I have found them in normal amount. Brattler¹ gives two cases of pleurisy with effusion, accompanied by high temperature. In one the daily excretion of chlorides amounted to 3 grms., and in the other to $8\frac{1}{2}$ grms. In empyema also, there is no diminution. I have seen a patient who had pneumonia, and in whom, during convalescence, return of fever and re-extension of the thoracic dulness occurred. No fluid was found on puncture, and it was concluded that he had a fresh extension of pneumonia. The chlorides, however, remained abundant, and ultimately an empyema was found.

In *acute phthisis*, even with a continuously high temperature, I have found no appreciable diminution of the chlorides. On the other hand, when pneumonia develops around a phthisical focus, the excretion falls rapidly. I am inclined to believe, however, that even in such a case the diminution does not occur to so marked a degree as in an idiopathic pneumonia; but on this point my observations are not sufficiently numerous to justify a very confident statement.

In *broncho-pneumonia* I have failed to find the diminution which some writers have asserted to occur. In several cases of that disease in children, in which I have examined the urine, chlorides have always been present.

The behaviour of the chlorides is of special help in those cases of pneumonia in which physical signs are either entirely absent, or are delayed in their appearance. In such cases the chloride diminution occurs as usual, and I have known it prove of great help in diagnosis. It is also a valuable aid in cases where a thorough physical examination cannot be made on account of the exhaustion of the patient.

It remains to be added that there are some conditions of the stomach, such, for example, as hypersecretion and dilatation, in which the chlorides in the urine are much diminished, or may even disappear. The possibility of such an occurrence must be borne in mind when making a diagnosis.

The question of the *prognostic value* of the behaviour of the chlorides in pneumonia may be briefly dismissed. Apparently it is of no value at all. Cases of pneumonia in which chlorides are totally

¹ *Op. cit.*, p. 48.

absent are not necessarily more severe than those in which the diminution does not reach such a degree. A consideration of the appended cases indicates this quite distinctly. Nor can one say that there is any necessary connection between commencing return of chlorides and commencing resolution. In at least two cases, I have known death to occur after the chlorides had begun to reappear in the urine.

SUMMARY OF CLINICAL FACTS.

1. During an attack of croupous pneumonia the chlorides in the urine are greatly diminished or may even entirely disappear.

2. A comparison of intake and output shows that, as far at least as the urine is concerned, a true retention of chlorides within the body takes place. The amount retained averages about 2 grms. of sodium chloride for each day of the disease.

3. The diminution lasts usually for one or two days after the crisis, and is succeeded by a sudden and excessive excretion, the amount of chlorides in the urine now rising considerably above that in the food.

4. The degree of the diminution varies considerably in different cases but bears no relation to the degree of fever present, to the extent of lung involved or to the presence or absence of albuminuria.

5. The chlorides are the only constituent of the urine which is diminished in pneumonia; the phosphates and sulphates tend, like the urea, to be increased.

6. Diminution of chlorides is not pathognomonic of pneumonia, but may occur in other acute fevers, notably in typhus and acute rheumatism, but is more constant in croupous pneumonia than in any other febrile disease. Examination of the urine is thus of negative rather than positive value in the diagnosis of pneumonia from other cases of acute pyrexia, the presence of abundant chlorides being opposed to the diagnosis of croupous pneumonia, though their diminution, or even their absence, does not necessarily imply that the case is an example of that disease. In cases of malaria the chlorides are actually increased during the febrile period.

7. As croupous pneumonia is the only pulmonary disease in which diminution of chlorides occurs to any appreciable extent, an examination of the urine may prove of great value in the diagnosis of pneumonia from other causes of consolidation of the lung, and from empyema, pleurisy, etc. It must, however, be borne in mind that the chlorides may be strikingly diminished in some cases of disease of the stomach, notably in dilatation.

8. The degree to which the chlorides are diminished is no criterion of the severity of the disease in any particular case, and is of no help in forming a prognosis.

PART II.—PATHOLOGICAL.

In this part of the present paper I propose to discuss the causes and explanation of the clinical facts regarding the chloride excretion in pneumonia which have already been described. And, first, the question has to be answered—

Does the Absorption of Chlorides go on normally in Pneumonia?

It was suggested by Traube⁽¹⁵⁾, as the cause of the disappearance of the chlorides from the urine, that the absorption of these from the alimentary canal was interfered with as the result of the fever. It must be admitted that this explanation is, *à priori*, extremely unlikely to be correct. One could hardly imagine a disorder of the stomach or intestines so profound as to entirely prevent the absorption of common salt. A definite reply, however, could only be furnished by estimating the amount of sodium chloride in the food and comparing it with the amount which appeared in the *fæces*. This has been done by Röhmann⁽⁴⁾, and his observations, which are confirmed by those of Terray, are so conclusive as to have rendered it unnecessary for the writer to perform any work in the same direction. Röhmann estimated the amount of sodium chloride in the diet of a normal individual, and compared it with the amount which appeared in the *fæces* in a corresponding period. He found that the *fæces* contained at most a few centigrammes of sodium chloride, and often a mere trace of that salt. In other words, sodium chloride was practically all absorbed. Similar observations on two cases of pneumonia gave the same result. The *fæces* were almost free from sodium chloride, and the amount of that salt contained in the food had been fully absorbed.

The next question which arises is this—

Is there any Vicarious Excretion of Chlorides during an Attack of Pneumonia?

It is conceivable that the chlorides might find their way out of the body by some channel other than the kidney, and so escape detection. We have just seen that the *bowel* cannot be regarded as such a channel of vicarious excretion. There remains the skin or such an abnormal vehicle as is furnished by the sputum.

The skin need hardly be considered. The cutaneous secretion is not necessarily increased in pneumonia, and in other diseases in which it is increased there is no disappearance of chlorides from the urine. Terray⁽⁶⁾, moreover, has been at the trouble to estimate the amount of chlorides in some of the sweat from a case of pneumonia. He found an amount of sodium chloride varying from 0·25 to 0·3 per cent., or not greater than the proportion in health.

The *sputum* is a vehicle of excretion which might at first sight be

overlooked. There are very few analyses of pneumonic sputum on record, but those show a surprisingly large amount of chloride.

Bamberger⁽¹⁶⁾ gives the following analysis of the ash constituents of various sputa, the figures being percentages of the ash :—

TABLE III.

	Bronchiec- tasis.	Chronic Tuberculosis.	Acute Tuberculosis.	Purulent Bronchitic Sputum.	Rusty Sputum, First to Seventh Days	Pneumonic Sputum during Resolution, Ninth to Twelfth Days
Cl	35	35	33	36	37	47
SO ₄	1	0·7	0·8	1	8	2·6
PO ₄	13	13	14	12	Trace.	1
K	22	24	19	20	41	14
Na	30	27	31	31	14	37
Ca	1	1·6	4	...	2	3·9

Beale⁽²⁾ has recorded the amount of sodium chloride in the sputum in some of his cases. He found it to vary from 4·3 up to as much as 18 per cent. of the solid matter. The more watery the sputum the larger apparently was the proportion of sodium chloride which it contained. He gives no analysis taken after the crisis. Terray⁽⁵⁾ gives the amount of sodium chloride in the sputum of twenty-four hours in one case, as 0·3 to 0·5 grms. before the crisis, and 0·4 to 0·5 after it.

I have made the following estimations in some of my own cases. In one case, in which there was typically rusty sputum, the following daily estimations were made :—

TABLE IV.

Day.	Weight of Sputum in Grms. Fresh.	Dried.	Percentage H ₂ O.	Total NaCl.	NaCl per Cent. of Dried Matter.
Fifth . . .	18	...	...	0·130	...
Sixth . . .	22	1	95·5	0·185	18·5 per cent.
Seventh . .	11	0·8	92·8	0·135	16·8 „
Ninth . . .	17·6	0·51	97·0	0·100	19 „

In another case the sputum was examined on the fourth day. It presented the typical pneumonic character, and 12·6 grms. were expectorated in twenty-four hours. The water amounted to 90 per cent. The solids contained 0·105 grms. of sodium chloride, or 16·6 per cent. of dried matter.

In another case, an examination on the sixth day gave 34 grms. of sputum, with 90 per cent. of water, and 0.230 grms. sodium chloride, or about 6 per cent. of the dried matter.

From an examination of these analyses, which accord well with those of Beale, it will be seen that pneumonic sputum is indeed very rich in sodium chloride. The proportion of the salt bears a much more constant relation to the fluid than to the solid constituents of the sputum. It becomes absolutely less in amount as the disease progresses, but, owing to the increasing wateriness of the expectoration, it is, when compared with the solid constituents, relatively increased in the later stages of the disease.

The relative richness of pneumonic sputum in common salt will be seen on comparison of it with the sputa in other conditions. Berzelius (quoted by Beale) gives the amount of sodium chloride in healthy nasal and tracheal mucus as 8.4 per cent. of the solid matter. Landenheimer⁽³²⁾ found in 100 c.c. of sputum, from a case of cancer of the lung, 0.383 gm. sodium chloride, and in a similar quantity of sputum from a case of early phthisis 0.590 gm.

In a typical case of chronic bronchitis I found that 9 grms. of dried sputum were expectorated in the course of a day, containing 0.8 gm. sodium chloride, or 8.8 per cent. of the dried matter.

The comparative richness of pneumonic sputum in sodium chloride, when that salt may be at the same moment entirely absent from the urine, is a fact of some interest to which I shall return later. Despite the amount of salt which it contains, however, the sputum in pneumonia cannot be regarded as an important vehicle of chloride excretion. The total amount is too small. In no case did I find more than 0.3 gm. sodium chloride excreted in the sputum daily, an amount which is quite insufficient to account for the quantity which disappears from the urine.

Do the Chlorides Accumulate in the Pneumonic Exudate?

Even before it had been definitely shown that any real *retention* of chlorides took place in pneumonia at all, the suggestion had been thrown out by Redtenbacher that these salts were "determined" to the site of the inflammation. This suggestion was adopted by Beale, who believed that he was justified, as the result of his analyses, in stating that the exudate in pneumonia is very rich in chlorides. This view has attained currency in the text-books and is not devoid of a certain probability. If the pneumonic exudate be really very rich in chlorides it seems natural that, during the progress of the inflammation, these should be withdrawn from the blood, and that their deficiency in the latter should find expression in the urine, while the reabsorption of the exudate after the crisis would easily account for the excess of urinary chlorides at that period. How much chloride, then, does the pneumonic exudate contain? On this point surprisingly few analyses

have been made. The conclusions of Beale rest only upon three. He found that the pneumonic lung contained 1·86 per cent. sodium chloride in the dried solids. The writer has made analyses of portions of the inflamed lung in six cases of pneumonia, at different stages of the disease.¹ The results are contained in the following table:—

TABLE V.—*Analyses of Pneumonic Lungs.*

Case.	Weight of Fresh Lung.	Weight after Drying.	Percentage of Water.	Percentage of Sodium Chloride in Dried Lung.
1. Apical alcoholic pneumonia with grey hepatisation . . .	46·8	8·97	80·9	1·05
2. Extensive grey hepatisation of lower lobe	58·5	10·4	82·1	1·66
3. Grey hepatisation, upper lobe .	51·9	9·6	82·4	1·67
4. Well-marked red hepatisation .	40·89	7·82	81	1·60
5. Advanced grey hepatisation .	7·38	1·55	79	2·0
6. Red and grey hepatisation . .	26·7	4·10	84·5	2·14
Average of six cases			81·6	1·69

For purposes of comparison the following analyses were made of non-pneumonic lungs:—

TABLE VI.—*Analyses of Non-Pneumonic Lungs.*

Nature of Case.	Weight of Fresh Lung.	Dried.	Percentage of Water.	Percentage of NaCl in Dried Lung.
1. Subacute nephritis	14·19	3·28	78%	1·4
2. Typhoid fever	4·53	0·855	81·2%	1·6
3. Unhepatised part of pneumonic lung	19·42	4·40	79%	1·3
Average			79·4%	1·4%

Beale² gives the average amount of sodium chloride in three specimens of pneumonic lung as 1·86 per cent. of the dried substance.

¹ The method of analysis was as follows:—A weighed portion of fresh lung was dried at 105° C. to constant weight. It was then slowly heated in a platinum capsule till all fumes had ceased to come off. The friable black residue was pulverised and extracted with boiling water; the residue was carefully incinerated with excess of soda and some saltpetre; the ash dissolved, and added to the original extract, and the chlorides estimated by Mohr's method.

² *Op. cit.*

Three healthy lungs gave an average of 1.16 per cent., or a difference of 0.7 per cent. in favour of the inflamed lung, as compared with 0.29 in my own analyses. Beale concluded from this difference that the chlorides go into the exudate. There is, however, a fallacy in this method of attempting to estimate the amount of chloride in the exudate. For, as Beale himself pointed out, the comparison is not really between equal bulks of lung (as it should be) but between equal weights of lung in two very different states. The analysis of healthy lung gives the composition of the lung plus a certain quantity of blood, while in the case of the hepatised lung the result represents the composition of the effusion along with that of a small and unknown amount of ordinary lung substance. But ordinary lung substance is itself very rich in chlorides, my own analysis giving an average of 1.4 per cent. of dried substance, while Nencki (¹⁷), in his tables of analysis of the relative amount of chloride in the different organs and tissues of the dog, ranks the lungs next to the blood, with an average of 1.2 per cent. of sodium chloride reckoned as the dry substance. Before we can tell the composition of the exudate, therefore, we must be able to tell approximately how much of the total amount of sodium chloride contained in the piece of inflamed lung belongs to the ordinary pulmonary tissue itself. I have attempted to obtain such information in the following way:—

A given bulk of pneumonic lung (say 4 c.c.) was measured off, cut away from the rest, dried and weighed. A normal lung was then taken and inflated to an extent corresponding to moderately full inspiration. A similar bulk was marked off upon the surface of this lung, and the piece cut out, after which, of course, it collapsed to almost half its volume. It was then weighed, dried, and weighed again. On comparing several pieces in this way it was found that the normal lung averaged 3.36 grms. (dry substance), while a similar bulk of pneumonic lung averaged 9.4 grms. In other words, of the weight of any given piece of pneumonic lung about one-third is due to the pulmonary tissue itself, and two-thirds to the exudate filling the air vesicles. Of 300 grms. of dried pneumonic lung, then, about 200 grms. represent the exudate. But from the averages already given, such a piece of lung would contain 5.28 grms. sodium chloride. But 100 grms. of ordinary pulmonary tissue contain 1.4 of sodium chloride. Therefore the remaining 200 grms. (*i.e.* the exudate) will contain 3.88 grms. of NaCl, or, in other words, the amount of sodium chloride in pneumonic exudate is 1.94 per cent. of the dried matter. Of course, this is merely an approximate calculation, based on the averages of the analyses made by the writer, and may, in individual cases, rise somewhat above or fall a little below this figure.

Since these estimates were made two analyses have been published by Terray,¹ where he was able to get the entire pneumonic lung for

¹ *Op. cit.*

examination, and he has compared with these the results yielded by two healthy lungs, which had been rendered almost free from blood. For convenience I have put his results in tabular form.

TABLE VII.

PNEUMONIC.			HEALTHY.		
Description of Lung.	Weight, Dry.	Total NaCl.	Description.	Weight, Dry.	Total NaCl.
Left; almost entirely consolidated	286 grms.	7·8	Left lung.	63·3	1·1
Right; entirely consolidated	301 ,,	10·28	Right lung.	151·2	3·1
Average in 100 parts of dried lung		3·05 %	Average in 100 parts of dried lung		1·85 %

Examining these results it is seen that in one case (left lung) the pneumonic only contained 6·7, and in the other (right) almost 7 grms. more of sodium chloride than the healthy lung, and yet these were cases of very extensive hepatisation. According to these figures 300 grms. of dried pneumonic lung would contain on an average 9·15 grms. sodium chloride. But of this amount of lung about one-third (*i.e.* 100 grms.) is, as we have seen, to be regarded as ordinary pulmonary tissue, and that would contain 1·85 sodium chloride, leaving 7·30 grms. sodium chloride in 200 grms. of dried exudate, or 3·6 per cent., a somewhat higher average than my own analyses yielded. Reviewing the whole of the evidence it is obvious that the amount of sodium chloride which is contained in the exudate in the inflamed lung will not account for the quantity which disappears from the urine in the course of a pneumonia. The exudate contains about 80 per cent. of water and only 2·4 per cent. of sodium chloride in its dry residue. A kilogramme of fresh exudate would therefore only withdraw from the blood 4 to 8 grms. of sodium chloride; and Terray found, even in lungs almost completely consolidated, only about 6 to 7 grms. of sodium chloride in the exudation. Inasmuch as the amount of sodium chloride kept back in the body in the course of a pneumonia may easily amount to 2 grms. for each day of the disease, it is evident that one must look elsewhere for the cause of the disappearance of the chlorides than to the pouring out of an inflammatory exudate rich in common salt.

It is of some interest to compare the analysis of the pneumonic exudate with that of pneumonic sputum already given. In the latter, it will be remembered, the sodium chloride present amounted sometimes to as much as 19 per cent. of the dried matter, and even the lowest sample showed an amount equal to nearly 5 per cent. This

difference in the composition of the sputum and of the exudate is very striking and would indicate that the sputum in pneumonia is not derived directly from the inflammatory effusion.

The comparatively small amount of sodium chloride present in the exudation in pneumonia is not really surprising. The chlorides of the body are chiefly contained in its fluids, but the exudation in pneumonia is by no means fluid, containing, in fact, no higher a percentage of water than does normal lung tissue.

The small percentage of chlorides present explains also the clinical facts that there is no traceable relation between the extent of a pneumonia and the degree to which diminution of the urinary chlorides occurs, and that, while a pleuritic effusion to the extent of 1 litre will contain about 6 grms. of sodium chloride, or almost as much as was found in an entirely hepatised lung, yet pleurisy with effusion is not usually accompanied by any striking diminution in the excretion of chlorides.

Are the Chlorides Retained because the Kidney is unable to excrete them?

This question has been replied to in the affirmative by a considerable number of writers. It was first propounded as a theory to explain the disappearance of chlorides by Fränkel⁽⁶⁾. He grounded it on the well-known disturbance of function of organs in fever and on the fact that, post-mortem, one often finds this disturbed function to have been associated with structural alterations. He believed that the kidneys were affected with special frequency in fever, and supported this opinion by reference to the frequent occurrence of albuminuria in febrile conditions, and the common existence of cloudy swelling of the kidneys after death. That toxic products are produced in fever, which have an irritating effect on the kidney, may be inferred also from some of the experiments of Bouchard.¹ He found that febrile urine when injected into rabbits was often followed by albuminuria, while normal urine scarcely ever had that effect.

There seems to be no doubt also that changes in the parenchyma of the kidney are very constantly found, post-mortem, in cases of pneumonia. Fränkel and Reiche⁽¹⁰⁾ examined the kidneys in forty-five fatal cases of pneumonia. In every case they found changes affecting the secreting tubules, Henle's tube, and the straight tubule. The changes consisted in a marked degree of cloudy or granular swelling. More rarely there was coagulation necrosis. In every case, too, there was some exudation into the capsule of the glomerulus, although the amount of it was found to vary very much in different instances. These changes they found even in cases which had shown no albumin in the urine during life.

On the other hand, it will be admitted that very similar changes would probably be found in almost any case of acute fever, and, as has

¹ "Leçons sur les auto-intoxications."

been shown, albuminuria is not a more frequent symptom in pneumonia than in other acute febrile diseases. There is, therefore, no conclusive evidence that the kidney function is specially impaired in pneumonia. But even had this been proved it is difficult to see how it could explain the diminution of chlorides. For whatever theory one may hold as to the exact method by which the saline constituents of the urine are excreted, it is difficult to believe that the kidney can ever have much difficulty in dealing with common salt. And it is even more inconceivable that the difficulty should occur in regard to common salt alone, and that, while the phosphates and sulphates are being got rid of in quantities even surpassing the normal, there should be an entire inability to deal with the chlorides.

The more recent supporters of the theory, however, found it upon experimental rather than clinical evidence. Thus Bachrach (¹⁸) has endeavoured to test the secreting power of the kidney in fever by observing the time required to eliminate iodide of potash as compared with the time required in health. He found that after subcutaneous injection of 0.05 grms. the excretion of the salt by the kidney did not begin for about thirty minutes, as compared with three to five minutes in health. Hecker (¹⁹) got similar results.

The obvious criticism on these experiments is that they merely show that excretion is delayed, not that it is abolished. It might be justifiable to infer from them that the excretion of chlorides takes place more slowly than in health, but not that it does not go on at all.

Klees (²⁰) has gone further than this. He has attempted to reproduce artificially a condition of "renal irritation" with albuminuria, and has studied its effects upon the excretion of chlorides. His experiments were performed upon rabbits and dogs. He injected subcutaneously a mixture of distilled water and glycerine, and got as a result the appearance of blood and albumin in the urine, which soon gave place to albuminuria only, which lasted a few days, and then disappeared. He gives tables showing the results of three experiments, and as his paper is written in the Dutch language, and is not easy of access, I have here reproduced one of these tables (Table VIII.). It will be noted that on the day following the injection the chlorides in the urine showed a marked diminution, and remained less than normal, while the albuminuria lasted, to be succeeded by an excretion surpassing the normal. This corresponds, according to Klees, with the diminished chloride excretion during the course of a pneumonia, and the excessive excretion of it after the crisis. During the period corresponding to the existence of acute renal irritation chlorides are retained in the body, the kidneys being unequal to their excretion. As the kidney gradually recovers its function the chlorides reappear, and the quantity retained now appears in the urine as an excess. I have repeated these experiments,

employing for the purpose rabbits. Five experiments were performed, 20 c.c. of a mixture of water and glycerine being injected subcutaneously in each case. In only one of these, however, did transient albuminuria appear. In all the others hæmoglobinuria was present for one day, but on the day following the urine was quite normal again. The results of the successful experiment are contained in Table IX.

It will be noted that on the day of the injection the amount of the urine was not diminished. It contained much blood pigment and albumin. The chlorides were estimated in it by incineration of 10 c.c. and titration by the method of Volhard. They amounted to

TABLE VIII. (Klees).—*Male Rabbit, 2178 grms. Constant Diet.*

Day of Month.	Urine.	Specific Gravity.	Albumin.	Cl per Cent.	Cl in Twenty-four Hours.	Urea per Cent.	Urea in Twenty-four Hours.	
18-19	225	1016	None.	0·5	1·125	...	...	...
20	265	1017	"	0·46	1·129	...	...	...
21	340	1018	"	0·54	1·836	...	...	...
22	250	1016	"	0·52	1·300	1·8	4·5	...
23	275	1015	"	0·54	1·485	1·7	4·6	...
26-27	72 (11-5 o'clock.)	1021	{ Blood and albumin	0·18	0·356	Lost.	...	{ At 11 o'clock on 26th, injection of 20 c.c. of glycerine and water.
	162 (5-11 o'clock.)	1023		0·14				
28	330	1014	Albumin.	0·16	0·528	1·7	5·6	...
29	275	1015	Trace.	0·3	0·825	2·2	6	...
30	350	1017	?	0·62	2·170	2·1	7·3	...
31	250	1018	None.	0·58	1·450	2·7	6·7	...
1	280	1020	"	0·52	1·456	2·6	7·2	...
2	290	1017	"	0·46	1·334	2·5	7·2	...

TABLE IX.—*Experiment on Artificial Production of "Renal Irritation" in a Rabbit, and its Effect on Excretion.*

Date.	Quantity.	Specific Gravity.	Total NaCl.	SO ₄ . ¹	Diet.	Remarks.
June.						
11-12	62 c.c.	1025	0·489	1·277	170 grms. cabbage	...
13	48 "	...	0·537	0·575	160 "	...
14	55 "	1030	0·341	1·259	170 "	...
15	35 "	1025	0·238	0·77	160 "	...
16	43 "	1026	0·098	0·301	27 " (=0·04 NaCl).	20 c.c. glycerine and water subcutaneously.
17	100 "	1020	0·200	1·35	110 grms. cabbage	Blood casts and much albumin.
18	55 "	1025	0·313	1·111	123 "	Trace of blood; 1 per cent. albumin casts.
19	70 "	...	0·581	1·491	145 "	No blood; still albumin; few casts.
20	54 "	1030	0·432	1·556	126 "	Trace of albumin.
21	85 "	1022	0·510	1·96	165 "	" "
22	57 "	1025	0·382	1·33	183 "	No albumin.
23	78 "	1032	0·452	2·34	187 "	" " ...

¹ SO₄ = BaSO₄.

0.098 grms. NaCl for the twenty-four hours. This was considerably less than the daily quantity prior to the injection, but, on the other hand, the animal was ill, and its appetite diminished, so that in the twenty-four hours succeeding the injection it ate only 27 grms. of cabbage as compared with 160 in the previous twenty-four hours. This quantity of cabbage contained 0.04 grms. NaCl, so that, as a matter of fact, the excretion of chloride had exceeded the amount ingested in the corresponding time. On the next day, when albumin was still abundant in the urine, the chlorides amounted to 0.2 grms., or almost exactly the amount contained in the diet; and on the succeeding day, albuminuria still being present, the chlorides had returned to fully the normal amount.

For purposes of comparison I estimated also the sulphates in the urine. A glance at the table will show that they behaved in an exactly similar manner to the chlorides, a state of things which is just the reverse of what occurs in pneumonia. The only other urinary ingredient, besides the chlorides, which Klees estimated, was urea, and unfortunately the amount excreted on the day of the injection is not stated. That the urea excretion on subsequent days was not much altered may be explained by the fact, which he mentions himself, that the glomeruli were apparently much more affected by the injection than the tubules, their epithelium being always separated from the capillaries by a space containing albuminous matter and sometimes blood pigment. That is to say, the channel which probably serves for the elimination of the mineral constituents of the urine was practically blocked up. This, however, is not comparable to the state of the kidney in pneumonia, in which the tubules are more profoundly affected than the glomeruli.

I think, then, that from experiments such as these no conclusion regarding the renal function in pneumonia can legitimately be drawn—first, because the nature of the kidney lesion is not the same in the two conditions; secondly, because I have found that even when albumin was present in the urine, to the extent of 1 per cent., there was found to be no inability to excrete as much chloride as was ingested; and, lastly, because there is no reason to believe that any alteration in the kidney function so brought about affects the excretion of one mineral constituent alone, and not all of them equally.

But it is not really necessary to have recourse to experiment to prove that the retention of chlorides in pneumonia is not due to any defect of power in the kidney. One has merely to inquire into the state of the urine in cases of acute renal inflammation. Bartels gives the analysis of the urine in one case of acute nephritis; it contained 4.5 grms. sodium chloride daily, yet both blood and albumin were present in abundance. Parkes⁽²¹⁾ gives a case in which, even when very severe inflammation existed, 2.7 grms. were present in the urine daily, and only when suppression of urine prac-

tically supervened did the chlorides sink to nil. He states, moreover, that he has always found the sulphates and phosphates diminished along with the chlorides, an observation which is confirmed by Salkowski and Leube⁽²²⁾.

Dickinson⁽²³⁾ states that in acute nephritis the chlorides are invariably diminished, sometimes totally absent, but he states also that phosphates and sulphates are diminished likewise. Von Noorden⁽²⁴⁾ asserts that sodium chloride in nephritis is only diminished when the urea itself is, and that he has never seen the former in small amount unless the urea was also diminished. My own observations would confirm these statements. As far as I have observed, the chlorides are not reduced to a greater extent in nephritis than the small amount ingested in the diet would account for.

On the whole, then, one must discard the theory that the diminished chloride excretion in pneumonia is due to impaired functional power on the part of the kidney, and the question which stands at the head of this section must be definitely responded to in the negative.

Do the Chlorides accumulate in the Blood?

Seeing that the amount of chlorides in the inflammatory exudate only accounts for a fraction of the quantity retained in the body, we have to look elsewhere for the remainder. And one naturally turns first to the blood.

Are the chlorides in the blood increased in pneumonia? I have not been able to obtain large quantities of blood for analysis from pneumonic patients, but have made comparative analyses of pleuritic effusions from such patients, and compared the results with those obtained in other diseases. That the composition of such an effusion is, as regards its saline constituents, quite a reliable index of the composition of the blood serum, has been shown by Runeberg⁽²⁶⁾. He analysed upwards of eighty-five exudations, and found a remarkable constancy in the amount of sodium chloride which they contained. "Any individual differences," he concludes, "are due to differences in the amount of the salts in the blood in that particular case," and this he proved by analysis of the blood serum and the exudate in each case, the two being always found to correspond.

On an average he found that inflammatory exudates contained 0.65 grms. sodium chloride per 100 c.c., while non-inflammatory contain 0.70 grms. The tables on the following page are my own results.

It will be observed that the proportion of sodium chloride is considerably lower in the pneumonic cases.

Laudenheimer⁽³²⁾ found in serum obtained from cases of pneumonia by tapping 0.58 to 0.60 per cent. sodium chloride, as compared with 0.64 per cent. in healthy serum.

Von Limbeck (³⁴) found in the serum of four healthy persons, 0·78, 0·78, 0·78, and 0·67 per cent. sodium chloride, and in three cases of pneumonia, 0·54, 0·61, and 0·68 per cent.

TABLE X.—*Non-Pneumonic Cases.*

Nature of Case.	Amount Analysed.	Per Cent. Water.	NaCl in 100 C.c.
Hydrothorax. . . .	25 c.c.	97·2	0·680
Ascitic fluid from cirrhosis of liver . . .	25 „	98·5	0·688
Pleurisy with effusion . . .	25 „	93·4	0·632
Average		96·3	0·666

TABLE XI.—*Pneumonic Cases.*

Case.	Amount Analysed.	Per Cent. Water.	NaCl in 100 C.c.
Typical alcoholic pneumonia with pleuritic effusion	10 c.c.	92·8	0·540
Extensive grey hepatisation with some effusion in pleura	15 „	93	0·585
Double pneumonia and pleurisy	10 „	94	0·545
Average		93·2	0·523

Runeberg (²⁶) gives the result of the analysis of blood serum in two cases of croupous pneumonia in which bleeding was resorted to. He found an average of 0·59 grms. sodium chloride per 100 c.c., as compared with an average in non-pneumonic cases of 0·66.

Analyses of the blood as a whole in cases of pneumonia are given by von Limbeck,¹ and by Moraczewski (³⁵). Both observers found a diminution in the amount of chlorides in the pneumonic blood. The latter found that after the crisis the amount of chlorides in the blood rises again.

There is thus a large amount of evidence to show that during an attack of pneumonia the amount of chlorides in the blood is diminished. Obviously, therefore, the retained chlorides do not accumulate in the blood.

The diminution of the chlorides in the urine, however, is out of all proportion to the degree of diminution found in the blood. In

¹ *Op. cit.*, p. 121.

the latter it only amounts to a decigramme or less in every 100 c.c., whereas in the urine the diminution may go the length of total disappearance. It seems almost incredible that the kidney function can be so delicately adjusted that such a slight fall in the amount of sodium chloride in the blood should lead to an entire cessation of its excretion. Certainly such an occurrence would be inexplicable on any merely physical theory of the renal excretion of salts. But it may be suggested that the chlorides in the blood during an attack of pneumonia are in a different condition from the normal. Halogen compounds with proteids are now well known, and it might be supposed that, in the altered metabolism of acute fever, some such compound was formed which fixes the chlorine and renders it incapable of excretion by the kidney. There can be almost no doubt, however, that the chlorides, wherever they disappear to, remain still chiefly in the form of sodium chloride. Salkowski⁽³⁰⁾ found that during the course of acute fevers the amount of sodium excreted is markedly diminished, while the amount of potassium is increased. He gives tables from cases of pneumonia, showing the relative amounts of sodium and potassium excreted prior to and after the crisis. In the precritical period potassium surpasses the sodium; after the crisis the reverse holds good. Now, as sodium in the urine is chiefly combined with chlorine, this would indicate that there is a relationship between the retention of chlorine and that of sodium, that, in fact, the latter is retained in the form of sodium chloride. Still, compounds of inorganic salts with proteids (*Salz-eiweiss-verbindungen*) are well known, and the sodium chloride in the blood might, during the pneumonia, get linked on to proteid, and so escape excretion. It is difficult to either prove or disprove the existence of such hypothetical compounds. I have attempted to settle the matter by the only way open, namely, by dialysis. It is reasonable to suppose that, if such compounds exist, it should be less easy to remove common salt from the fluids containing them by dialysis than it is in the case of ordinary serum. I compared the behaviour, in this respect, of serum derived from a pleuritic effusion, occurring in the course of an attack of croupous pneumonia, with that of an ordinary (non-pneumonic) effusion. A definite quantity of each fluid was taken and placed in a dialyser in distilled water. The water was changed at intervals of twenty-four hours, and the amount of chlorides in it estimated. Dialysis was continued in each case till the dialysate was free from salt. I found, however, as the result of several trials, that there was no appreciable difference between the rate of dialysis in the two cases. Equal proportions of sodium chloride passed through in corresponding times, and after three days the original fluid in each case contained mere traces of common salt.

On the whole, therefore, one concludes that the chlorides retained in pneumonia do not accumulate in the blood, nor can their failure

to be excreted be explained by the assumption that they are present in that fluid in an unusual form of combination.

Do the Retained Chlorides accumulate in the Fixed Tissues or in any Particular Organ?

Of the fixed tissues one may select the muscles as most suitable for examination. Curiously enough there are not many analyses of muscle available to give one a standard for the normal amount of chloride found in them.

Nencki (¹⁷) gives the amount of sodium chloride in the muscles of the dog as varying from 0.198 to 0.258 per cent. of the dried matter. Katz (³³) gives a very elaborate series of analyses of the mineral constituents of the muscles from different animals. He examined one sample of human muscle and found it to contain 0.413 per cent. sodium chloride in the dried substance.

I have analysed two samples of muscle (biceps), one from a case of apoplexy, the other from a case of carcinoma of the stomach. The former contained 58 per cent. of water and had 0.283 per cent. sodium chloride in its dried substance; the latter had 75 per cent. of water, and 0.216 per cent. sodium chloride in the dry matter. The average of the two was 0.249 per cent. sodium chloride in the water-free substance.

One may compare with this the results of the analyses of samples of biceps in three typical cases of pneumonia:—

TABLE XII.

Case.	Water.	NaCl per Cent. of Dried Substance.
1. Apical pneumonia—stage of grey hepatisation . . .	83	0.266
2. Basal pneumonia . . .	74	0.233
3. „ „ stage of red hepatisation.	77	0.316
Average . . .	78	0.271

The average is higher in the three cases of pneumonia.

Moraczewski (^{35c}) gives analyses of heart muscle in pneumonia. He found in one case 0.82 per cent., and in another 2.18 per cent. *chlorine* in the dried substance, as compared with 1.05 per cent. in a case of death from hæmorrhage, and 0.255 per cent. in a “normal” case.

It will be observed that the results given by different observers even in normal cases show very considerable variations in the amount of chloride present, but on the whole evidence one may say that the

amount of chlorides in the fixed tissues in pneumonia is not diminished, but, on the contrary, probably somewhat increased.

Of individual organs, the liver, owing to the observations of Bohne ⁽³⁶⁾ on the accumulation of sodium chloride in the liver in cases of coma, seemed specially to merit investigation. In order to get a standard of comparison, I analysed a series of livers taken consecutively from the post-mortem room. The organ was cut into thin slices and all blood squeezed out as far as possible. It was then chopped up, dried, ground to a powder, and incinerated with quicklime in a tube. After solution and filtration of the ash, the chlorides were precipitated with nitrate of silver, and weighed. The results are contained in the following table:—

TABLE XIII.—*Analyses of Livers from Non-Pneumonic Cases.*

Case.	Per Cent. Water.	Per Cent. NaCl in Fresh Substance.	Per Cent. NaCl in Dry Matter.
1. Phthisis . . .	76·6	0·177	0·76
2. Suspected typhoid .	75·5	0·218	0·89
3. Tuberculosis (child, æt. 8 years) . . .	82	0·136	0·76
4. Fatty heart . . .	71·3	0·272	0·95
5. (?)	73	0·162	0·60
Average .	75·6	0·193	0·792

The next table shows the results obtained by a similar examination of the liver in a series of cases of pneumonia:—

TABLE XIV.—*Analyses of Livers from Cases of Pneumonia.*

Case.	Per Cent. Water.	Per Cent. NaCl in Fresh Liver.	Per Cent. NaCl in Dried Liver.
Croupous pneumonia, male, æt. 43 .	75	0·250	1·0
„ „ „ 50 .	74	0·247	0·95
„ „ „ 35 .	77·3	0·172	0·75
Double lobar pneumonia .	77·4	0·140	0·62
Average .	75·9	0·202	0·830

Here again it is seen that the comparison, as regards amount of chloride present, is rather in favour of pneumonic cases.

Analyses of the liver and also of the other organs (kidney, spleen, etc.) in cases of pneumonia and other diseases are also given by Moraczewski (^{35 c}), for which his original papers must be consulted. He found, however, in harmony with the above results, that the organs in cases of pneumonia tended to be richer in chlorides than normally. We may therefore conclude that the chlorides which are retained in cases of pneumonia accumulate in the fixed tissues and in the organs generally, while they disappear, to some extent, from the body fluids.

Does Retention of Chlorides occur in Fevers induced experimentally?

I have investigated this point on rabbits by the production of *Pneumococcus septicæmia*. In each experiment death followed, and the pneumococcus was found in the blood, but in none did any reduction in the amount of chlorides in the urine occur. I tried, also, the injection of cultures of the bacillus of pseudo-tuberculosis and the intravenous injection of putrid matter, but although the rectal temperature rose sometimes to 105° F., no chloride retention occurred.

A similar want of success has attended the efforts of other experimenters. Thus Schenck (²⁷) succeeded in raising the temperature of a dog to 42° C. by the injection of putrid matter, whilst Klees (²⁰) produced evanescent fever (39° to 40° C.) in rabbits by the injection of helleborin; but in neither case did any reduction in the chloride excretion follow.

One is, therefore, unable to study the pathology of the subject experimentally, but must confine himself to clinical facts.

DISCUSSION OF RESULTS.

Having tracked down the chlorides and found that they accumulate in the fixed tissues and organs generally, it remains to be discussed why this should occur. And, first, it may be pointed out that a similar occurrence takes place during chloride starvation. Schenck (²⁷) experimented upon dogs and rabbits, and found that on chloride-free diet the amount of sodium chloride in the blood sank greatly during the first few days, but soon began gradually to rise again until it almost reached the normal once more. His explanation is that at first chlorides leave the blood and pass into the solid tissues, but that by and by equilibrium is again established and a return to the blood follows. There is thus, as it were, a balance between the blood and the tissues as regards chlorides; and when there is a scarcity of the latter, or when there is a greater need for them in the body, they seem to be withdrawn from the blood and hoarded up in the tissues, and this is what appears to occur in acute fevers and especially in pneumonia.

Forster (²⁰) propounded the idea that the salts of the body are to be regarded as belonging to two categories—(1) salts which are uncombined and circulate freely in the blood; and (2) salts which are

firmly combined with organic substances in the fixed tissues and also in the blood. He found that in animals which were put upon a chloride-free diet, the amount of chlorides in the urine rapidly fell to a mere trace. If, however, food were now withheld altogether for a day, the amount of chlorides in the urine on the following day was considerably increased, even although the diet was still free from salt. His explanation of this phenomenon is that in hunger the fixed tissues are broken down and their organically combined chloride is liberated and appears in the urine.

Röhmnn (⁴) tried to adapt this view to explain the behaviour of the chlorides in pneumonia. He supposed that in that disease a great destruction of fixed tissues occurs. The liberated organic matter gains access to the blood, and there fixes on to the free chloride, so that the latter enters into organic combination. To this view it may be objected—(1) that it presupposes that when the fixed tissues break down they do not carry with them into the blood enough salt to combine with their proteid matter; (2) that in any case the organic matter would not remain in the blood, but would be broken down and the chloride liberated; and (3) that my own observations do not show that the chlorides in the blood are in a different form of combination in fever from that in health.

The view has been maintained by Laudenheimer (³²), Terray (⁵), Moraczewski (^{35 c}), and others, that in all cases where a retention of chlorides within the body occurs, it will be found that water is also retained, and that the chlorides are only made use of to form a normal salt solution with the water. This view attaches a minor importance to the retention of chlorides, and makes the accumulation of water in the body the chief pathological fact. That water is retained in the body during fever was first asserted by Leyden (²⁵), and he was induced to come to that conclusion mainly by a study of the alterations in weight which patients undergo during and after an acute fever such as pneumonia. Terray and Laudenheimer have attempted to estimate the amount of water held back, and to show that it would just about suffice to make a normal salt solution with the quantity of salt retained during the same period. But their figures are very unconvincing. For, in the first place, they were only able to estimate accurately the amount of water excreted by the kidneys, the quantity eliminated by the skin and lungs being merely guessed at. And although there may be no reason to believe that the amount of insensible perspiration is increased in pneumonia (³⁷), yet there is every reason to suppose that the increased rapidity of respiration will cause a great increase in the amount carried off by the lungs.

It is difficult to decide the question by direct estimation of the amount of water in the tissues of persons dying of pneumonia as compared with the amount in health. Moraczewski¹ admits that

¹ *Op. cit.*

there is no evidence that the amount of water in the blood is increased in pneumonia, but thinks, as the result of his own observations, that there is a higher percentage than normal in the tissues. In the analyses which I have made of muscle from cases of pneumonia, I certainly found a higher percentage of water (78 per cent.) than is given by Katz as the normal, from an average of numerous observations on muscle in health (76 per cent.). But the difference is not great, and its constant occurrence could only be established by a very large number of observations. When one reflects, moreover, that the retention of 12 grms. of sodium chloride, an amount which may easily be reached in the course of a pneumonia, would suffice to form about 20 litres of a fluid which would have the same percentage of salt as lymph, one can hardly believe that all the salt retained simply goes to form a normal salt solution, even were there not opposed to that view the fact that there is no similar retention of the other saline constituents of the blood. Lastly, there must be urged against this theory the fact that if one administers salt to patients with pneumonia it also is retained. I have given in this way as much as 2 drms. of salt to a patient with pneumonia in the course of twenty-four hours, without observing any increase in the amount excreted (see Case 5).

All these facts are opposed, in my opinion, to the view that sodium chloride is retained in order to form a normal salt solution, and make rather for the belief that the chlorides are kept back for their own sake.

Why chlorides should pass into the fixed tissues in acute fever, it would be very difficult to say. It may be that the increased metabolism associated with fever necessitates somehow the presence of abundance of sodium chloride. Thus Kast⁽³¹⁾ has shown that in healthy dogs poisoning with carbonic oxide is accompanied by some degree of chloride retention, and a greatly increased tissue metabolism is the result of carbonic oxide poisoning (Fränkel). On the other hand, there is the difficulty that retention of chlorides is not by any means equally marked in *all* cases of fever. One could understand why it does not occur in chronic fever, because an equilibrium between the blood and the tissues would have time to be established again in such cases, but even in many acute fevers retention does not occur very markedly. Of these malaria is, as we have seen, a conspicuous example, the chloride excretion being actually increased during the febrile period in that disease.

It has been attempted by Terray, Schenck, and others to explain this exceptional occurrence by the assumption that there is a great destruction of red corpuscles during the febrile period in malaria, and that the increased amount of chlorides excreted is derived from these. They support this view by the results of the experiments of Kast, who found that in dogs the injection of toluylenediamin is followed by an increase in the urinary chlorides. The validity of this explanation is,

however, extremely doubtful. In the first place, the red cells are poor in chlorides, and any destruction of them likely to occur could hardly affect to an appreciable extent the amount of chlorides in the urine. Kast himself admits that the increased excretion, which followed the injection of toluylenediamin, was considerably greater than could be accounted for by any destruction of red corpuscles alone, and that it must have acted in some other way as well. Further, in one case of paroxysmal hæmoglobinuria which I have investigated, I found no increased excretion of chloride during the paroxysm, and the same was true of the four cases of experimental hæmoglobinuria in rabbits, to which allusion has already been made.

For my own part I think it is much more likely that the anomalous behaviour of the chlorides in malaria is to be explained by the marked diuresis which occurs during the febrile period of that disease. This diuresis is probably caused by the great contraction of the cutaneous vessels, which characterises the "cold stage" of the malarial attack. The increased excretion of water carries with it the urinary solids, and these are all found to be increased, the chlorides among the rest. A very similar explanation has been recently advanced by Rem and Picci (³⁸), as the result of a careful study of the chloride excretion in thirteen uncomplicated cases of malaria.

It is also very probable that the retention of water, which Leyden has shown to occur in acute fevers, is due to a lowered arterial pressure in the kidney, causing a diminished filtration from the blood plasma. This would account for the retention of a small amount of sodium chloride, but is not nearly adequate, as I have endeavoured to show, to account for the very great retention of that salt which is so characteristic of pneumonia.

SUMMARY OF PART II. (PATHOLOGICAL).

1. The absorption of chlorides from the alimentary tract goes on normally in acute fevers, and no vicarious excretion occurs by the skin, bowel, sputum, or other channel.

2. The sputum in pneumonia is very rich in sodium chloride, containing sometimes as much as 19 per cent. in the solid matter, but in spite of this fact the total amount excreted daily in the sputum is small.

3. The inflammatory exudate contains from 2 to 4 per cent. of sodium chloride in its solid matter, or not more than three times as much as the same weight of normal lung. It is thus not really very rich in chlorides, and the amount of the latter contained in the whole exudate will not account for more than one-third to a half of the total amount of sodium chloride retained in the body during an attack of pneumonia.

4. The difference in composition between the exudate and the

sputum indicates that the latter is not derived directly from the former.

5. The theory that the chlorides are retained because of a temporary functional disability on the part of the kidney to excrete them, is negatived alike by the results of experiment and by a comparison of the composition of the urine of pneumonia with that of acute nephritis, where diminution of excretory power undoubtedly exists.

6. Examination of the blood from cases of pneumonia shows that the chlorides in it are diminished, but there is no evidence that they are present in any unusual form of combination. Their failure to appear in the urine must be attributed to the very delicate adjustment of the amount excreted by the kidney to the amount contained in the blood at the time.

7. There is no evidence that the chlorides tend to accumulate in any particular organ in pneumonia, but, on the other hand, all the organs and the fixed tissues in general, seem to be somewhat richer in chlorides than normally.

8. Attempts to produce chloride retention in pyrexia, artificially induced by the injection of the pneumococcus and by other means, have failed.

9. As to the reason for the passage of chlorides out of the blood into the fixed tissues in pneumonia, one can merely speculate, and the subject is fully discussed in the latter part of this paper. The writer is unable (for various reasons given) to agree with the view that the chlorides are retained secondarily, and as the result of the retention of a considerable quantity of water. The increased excretion of chlorides in malaria is probably to be attributed to increased arterial pressure in the kidney during the pyrexial stage of that disease.

PART III.—PROTOCOLS OF CASES.

NOTE.

The observations in Cases 1, 2, 3, 7, and 8 are exhibited in both tabular and graphic forms; in Case 5 a table is alone given, and in Cases 4 and 6 a chart only. The figures at the left-hand margin of the charts indicate grms.

The chlorides were estimated by the method of Volhard; the phosphates by titration with uranium acetate, ferrocyanide of potash being used as indicator.

All quantities are stated in grms., and all chlorine is represented as NaCl.

In those Cases (3, 5, 7, and 8) in which the intake of chlorides was also investigated, the diet was restricted to as few ingredients as possible, and the amount of chloride estimated in samples of these by careful incineration and titration by Mohr's method.

TABLE XV.—CASE 1—W. H., ÆT. 12.—*Croupous Pneumonia, Right Base, Extent doubtful (see also Chart 3).*

Date.	Day of Disease.	Quantity of Urine.	Specific Gravity.	Total NaCl.	Total P_2O_5 .	Remarks.
May 6 .	3rd	455 c.c.	1030	0·273 grms.	2·63	Milk and beef-tea only.
„ 7 .	4th	398 „	1028	0·079 „	2·58	...
„ 8 .	5th	759 „	1030	0·080 „	1·82	Crisis.
„ 9 .	6th	625 „	1025	0·312 „	1·75	...
„ 10 .	7th	1392 „	1010	0·696 „	1·80	...
„ 11 .	8th	824 „	...	3·048 „	1·56	Light diet from this date.
„ 12 .	9th	1164 „	1018	7·806 „	1·74	...
„ 13 .	10th	966 „	1020	6·085 „	2·89	...
„ 14 .	11th	1477 „	1014	13·293 „	2·51	...
„ 15 .	12th	710+ „	1020	7·1+ „	2·1	...
„ 16 .	13th	1051 „	...	6·306 „	1·15	...

TABLE XVI.—CASE 2—M. F., ÆT. 45.—*Croupous Pneumonia with well-marked Crisis, but Equivocal Physical Signs (see also Chart 1).*

Date.	Day of Disease.	Quantity of Urine.	Specific Gravity.	Total NaCl.	Total P_2O_5 .	Remarks.
June 6 .	7th (?)	670+	1012	2·34+	0·73+	Temperature, 104° (morn- ing), 102° (evening). Trace of albumin.
„ 7 .	...	1739	1018	2·60	3·9	Temperature, 100°, sub- normal. Trace of albumin.
„ 8 .	...	852	1025	Trace.	2·55	Temperature subnormal. No albumin.
„ 9 .	...	1130	1022	2·26	2·54	Temperature subnormal.
„ 10 .	...	?	1020	9+	3·16+	Normal.

TABLE XVII.—CASE 3—J. G., ÆT. 28.—*Prolonged Pneumonia associated with (?) Malaria. Consolidation began at Base and spread slowly upwards. Chlorides present throughout Attack (see also Chart 5).*

Date.	Day of Disease.	Quantity of Urine.	Specific Gravity.	P ₂ O ₅ .	NaCl in Urine.	NaCl in Food.	Remarks.
June 26 .	?3rd	1186	1022	2	2·04	?	...
„ 27 .	4th	1165	1022	3·26	0·69	4·82	...
„ 28 .	5th	1449	1022	2	2·17	5·23	...
„ 29 .	6th	1420	1020	2·41	3·12	5·65	...
„ 30 .	7th	1931	1020	4·17	4·82	7·56	...
July 1 .	8th	1930	1020	3·20	6·02	5·12	...
„ 2 .	9th	1846	1020	3·32	5·53	6·34	Sputum clearing.
„ 3 .	10th	2272	1020	4·55	6·81	5·65	...
„ 4 .	11th	2215	1018	4·20	6·64	5·5	Temperature now normal.
„ 5 .	12th	2220	1012	3·01	6·5	6·0	...
„ 6 .	13th	3237	Specimen lost.		7·5	...	...
„ 7 .	14th	1533	...	...	7·5	...	...
„ 8 .	15th	1732	1013	3·49	10·39	7·5	...
„ 9 .	16th	1533	1016	3·67	9·1	8·0	...
„ 10 .	17th	1136	1020	...	8·29	...	...
„ 11 .	18th	852	1020	1·95	5·36	...	Got up.
„ 12 .	19th	965	1018	...	8·39	...	...

TABLE XVIII.—CASE 5—H. G., ÆT. 39.—*Croupous Pneumonia (Alcoholic) Middle Lobe of Right Lung with few Physical Signs. NaCl totally absent.*

Date.	Day of Disease.	Quantity of Urine.	Specific Gravity.	NaCl in Food.	NaCl in Urine.	P ₂ O ₅ in Urine.	Remarks.
July 1 .	? 2nd	1420	1020	...	None.	0·065	Temperature, 105° F. Albuminuria.
„ 2 .	3rd	1435	1020	3·39	„	0·070	Temperature, 101°–102° F. Albuminuria.
„ 3 .	4th	1420	1022	3·99	„	0·120	Temperature, 103°–105° F. Less albuminuria.
„ 4 .	5th	1710	1020	2·88 + 2	„	0·138	Temperature, 102°–102° F. Salt given by mouth.
„ 5 .	6th	1567	1020	2·38 + 2	„	0·135	Temperature, 102°·4–102° F. Salt given by mouth.
„ 6 .	7th	...	1020	? + 2 grms.	„	0·105	Temperature, 103°–100° F. Died.

TABLE XIX.—CASE 7—P. M., ÆT. 25.—*Croupous Pneumonia. Consolidation of Left Upper Lobe (see also Chart 7).*

Date.	Day of Disease.	Quantity of Urine.	NaCl in Urine.	NaCl in Food.	Remarks.
July 13 .	5th	909 c.c.	None.	1·19	...
„ 14 .	6th	1250 „	Trace.	3·38	...
„ 15 .	7th	1818 „	2·727	1·406	...
„ 16 .	8th	1306 „	2·612	2·815	...
„ 17 .	9th	739 „	1·478	4	...
„ 18 .	10th	1136 „	9·769	5 (approx.)	Crisis.
„ 19 .	11th	740 „	3·288	„	...
„ 20 .	12th	1363 „	(Lost.)	„	...
„ 21 .	13th	1500 „	9·975	5·8	...
„ 22 .	14th	1676 „	10·5	6·5	...
„ 23 .	15th	2272 „	21·385	6·75	...
„ 24 .	16th	1818 „	14·08	7·8	...
„ 25 .	17th	3019 „	17·07	8·4	...

TABLE XX.—CASE 8—D. K., ÆT. 38. —*Pneumonia, Right Base, Extent Uncertain (see also Chart 6).*

Date.	Day of Disease.	Quantity of Urine.	NaCl in Urine.	NaCl in Food.	Remarks.
July 11 .	2nd (?)	1263	Trace.	2·5 grms.	...
„ 12 .	3rd	1220	...	...	Delirious.
„ 13 .	4th	894	Slight trace.	1·08 grms.	„
„ 14 .	5th	681 +	...	1·08 „	...
„ 15 .	6th	600 +	0·5 +	1·44 „	...
„ 16 .	7th	1050 +	1·2 +	2·88 „	Crisis.
„ 17 .	8th	1235	2·3	2·88 „	...
„ 18 .	9th	922	5·11	3·06 „	...
„ 19 .	10th	1490	...	2·34 „	...
„ 20 .	11th	1136 +	...	3·58 „	...
„ 21 .	12th	795	6·47	3·76 „	Resolution begin- ning.
„ 22 .	13th	780	5·14	4·30 „	...

CHARTS.

CHART 1.—Showing temperature and chloride excretion. (Case 2, Table XVI.)

CHART 2.—Showing temperature and chloride excretion. (Case 4.)

CHART 3.—Showing the temperature and the chloride and phosphate excretion. (Case 1, Table XV.)

CHART 4.—Showing temperature at crisis and chloride excretion. (Case 6.)

CHART 5.—Showing temperature and parallel curves of intake and output of chlorides and the phosphoric acid excretion in Case 3. (See also Table XVII.)

CHART 6.—Showing comparison between intake and output of chloride before and after crisis. (Case 8, Table XX.)

CHART 7.—Showing intake and output of chlorides before and after crisis in Case 7. (See also Table XIX.).

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