of the food. The fear of cold intensifies the ill effects of the indoor environment.

In the preparation of this paper I have been assisted by Dr. Novakovsky, who has collected evidence from numerous books on Eskimos and Lapps, and from Russian and other sources.

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HEPATIC INSUFFICIENCY IN SCARLET FEVER

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Nephritis is one of the most frequent and serious complications of scarlet fever. There are, in addition, cases in which, though no frank nephritis develops, symptoms and signs point to some involvement of the urinary system. At present there is no method by which the onset of this complication may be anticipated, and treatment must wait until symptoms develop, and may even then be half-hearted on account of doubt as to the diagnosis. It was therefore decided to carry out a careful clinical examination of cases of scarlet fever as a routine in the hope that some warning might be detected in the cases which later developed nephritis.

Investigation

The material was drawn from cases admitted to Belvidere Isolation Hospital in which a diagnosis of scarlet fever had been made. In each instance this diagnosis was confirmed by two medical officers. The number of cases investigated was 219. These were divided into three series.

Series 1 (63 Cases).—All were well-marked cases of scarlet fever, no mild or atypical ones being included. The investigation was carried out from the time of admission until the day on which the patient was allowed up (this was normally the twenty-first day of illness). Twelve of the sixty-three developed nephritis.

Series 2 (144 Cases).—Here all cases of scarlet fever admitted to the hospital over a period of three months were included, and the investigation was carried out for four to five days in the third week of illness. Seven in this series developed nephritis.

Series 3 (12 Cases).—These cases were all on a diet poor in protein (2.5 grammes daily) during the investigation, which was carried out for five days.

It was observed that the relation between the specific gravity and the urea concentration of a specimen of urine varied in a rather significant manner. The results have therefore been analysed from this aspect. Normally the specific gravity of urine varies with changes in the amount of urea in the urine, as a large proportion of the total dissolved solids of the urine is in the form of urea. It was considered that if some equation could be found to express this relation it might be of value in assessing the composition of the urine. The following equation has been suggested, and has been used in comparing the results of the cases:

The percentage of urea in the urine, multiplied by 10, minus the last two figures of the specific gravity estimation of the same specimen: the figure thus arrived at has been called the urea factor of a specimen of urine.

Example: If in a specimen of urine the percentage of urea is 2 and the specific gravity 1020, the urea factor is found as follows:

$$2 \times 10 - 20 = 0$$

This urea factor depends upon the proportion of the urea in the dissolved solids in the urine. This arbitrary figure was found to be normally about zero.

Results

It was observed that there was a general fall in the urea factor throughout the first three weeks of the illness, and that the figure was at its lowest at the critical period—that is, at the period when nephritis most commonly

CHART I

CHART I: SERIES 1 CASES.—This shows that there is a steady fall in the urea factor until the nineteenth day, and that thereafter it rises slightly. The lowest figure is -2 on the nineteenth day.

CHART II

CHART II: SERIES 2 CASES.—Here there is a fall from the seventeenth to the eighteenth day, and then the figure remains almost steady until the twenty-first day. The lowest figure reached is on the twenty-first day, and is 1.1.

CHART III

CHART III: NEPHRITIC CASES.—Here the urea factor is much lower than in the previous two charts. The lowest figure reached is -5.2.

CHART IV

CHART IV: SERIES 3 CASES.—Here the figure is seen to remain above zero although the patients were on a low protein diet.

occurs, namely the end of the third week. In cases with nephritis, however, the urea factor was found to be lower than in the non-nephritic cases. This fact is best seen by an examination of the accompanying charts.

The first chart shows the average urea factor for each day of illness in the cases in Series 1. The second chart shows the average urea factor for each day in the cases in Series 2. The days given here are necessarily only the seventeenth to the twenty-first. The third chart shows the average urea factor in the cases which had developed nephritis. The days in this chart are taken as starting on the day of diagnosis of the nephritis. The fourth chart shows the average urea factor in the cases in Series 3 for the five days when on a low protein diet. It must be remembered that the patients in Series 1, being selected as well-marked cases of scarlet fever, were, taken as a whole, more severely ill than those in Series 2.

Discussion

An interesting point is revealed by the examination of the urea factor. It is found that the figure falls progressively throughout the illness, until on the nineteenth day it reaches the lowest point, possibly tending to rise thereafter. The urea factor depends on two tests—the determination of the specific gravity of the urine and the percentage of urea in the same specimen of urine.

The specific gravity of water is 1000, while that of urine is normally between 1012 and 1024 (Cole, 1919). The difference between the figure for water and that for urine is accounted for by the dissolved solids in the urine. The percentage of urea in the urine is the amount per 100 c.cm. of urine. The urea factor is obtained from a figure derived from the dissolved solids in the urine and that derived from the urea in the urine. It is a figure indicating the proportion of the dissolved solids in the urine in the form of urea. A low urea factor signifies that instead of the urea forming approximately 80 per cent. of the urinary solids as in the normal (Hutchison and Rainy, 1924), it comprises a much lower percentage, and the proportion of some of the other solids must be increased or some other solid introduced. That means that there is either a diminished formation of urea or a diminished excretion of urea with possibly the excretion of another solid in its place. An increase in the excretion of ammonia in the urine occurs in acidæmia. In the cases in this series there were, however, no signs or symptoms of acidæmia and no apparent reason why it should occur. It should be noted here that the twelve cases on a diet poor in protein (Series 3) all showed urea factors within the normal limits, and that not all cases on a nephritic diet gave low urea factors.

Would a damaged kidney, if unable to excrete urea, excrete another solid in its place, or would the urea which it was unable to excrete be changed and excreted in another form? It is considered that it is more probable that there is a diminished formation of urea and an increased excretion of ammonium salts to keep up the elimination of nitrogenous waste products. With regard to this diminution in the formation of urea, Cole (1919) has shown that on starvation the percentage of urea in the urine falls and that of ammonia and creatinine rises. He also stated that in hepatic disease the percentage of urea falls and the excretion of ammonia is increased. That there is some hepatic involvement in scarlet fever is known, and attention to this fact has been drawn by Rolleston (1929), who says that, although it is unusual to find any obvious signs of hepatic disturbance, a slight involvement of the liver is present in almost every case.

The urea is formed almost exclusively in the liver so far as is known at present. It is therefore quite natural to find that disturbance of liver function gives rise to diminished urea formation. In scarlet fever it is known

that there is some hepatic involvement, and therefore there is possibly some diminution of urea formation. This would explain the urea factor. The urea factor is lowest in cases of nephritis, and therefore the hepatic disturbance is presumably more pronounced in these cases. Is it possible that the converse is true and that it is in the cases with the most marked hepatic involvement that nephritis develops?

If the above is a true assumption, I would suggest that this gives some explanation of the fact that nephritis is most liable to develop about the end of the third week. It is seen from the urea factor charts that the lowest point is at the end of the third week—that is, the liver function is at its lowest at this time. In some cases it is abnormally low, and in these one may expect nephritis to develop.

Summary and Conclusions

A clinical test of hepatic function is proposed, employing the specific gravity of the urine and the percentage of urinary urea. It is termed the urea factor. It is suggested that the hepatic function is low in the third week in scarlet fever and that this has a bearing on the development of nephritis. The conclusions to be drawn are:

1. The urea factor is of value in the prognosis of scarlet fever.
2. There is hepatic insufficiency in scarlet fever, and this is related to the development of nephritis.

I wish to thank Dr. T. Archibald for permission to carry out the investigation.

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Clinical Memoranda

Argyria due to Intranasal Medication

Generalized silver poisoning has become a rare condition since the internal use of silver preparations fell out of fashion. The case here reported was due to nasal medication over a long term of years, and demonstrates the danger of intranasal medication carried out without constant supervision.

CASE REPORT

The patient, an unmarried woman aged 61, was operated upon for a cleft palate at the age of 5. She has suffered all her life from migraine, and for the last twenty-five years has been taking phenacetin, 4 grains, caffeine, 1 grain. She sometimes took several powders daily, and recently has taken 100 a month. For the last ten years she has suffered from nasal catarrh associated with deafness, for which a nasal spray was prescribed shortly after the catarrh began; the spray has been used three times a day ever since. About four years ago she first noticed a greyish discoloration of the skin below the eyes, and this had gradually increased in intensity and extent. In August, 1938, after a severe bilious attack, she was advised to throw up her work as a companion and to return to Scotland.

Examination.—The patient was a small woman, thin but not emaciated, weighing 6 st. 2 lb. She was active, intelligent, and brisk in manner. Her skin was a remarkable blue-grey colour, the pigmentation being most pronounced over exposed parts, particularly on the cheeks below the eyes. The nipples and the nail-beds of the fingers were very distinctly blue. The hands and forearms showed the discoloration more than