lihood there is of obtaining a positive reaction to trichophytin. Positive reactions bear no relation to the findings of a positive culture or to the degree of severity of the clinical manifestations.

TREATMENT

The treatment of the affected children was along conventional lines, those requiring active treatment presenting no particular problem. Emphasis was placed rather upon prophylaxis. Boiling of towels and bathmats was insisted upon. In addition, footbaths containing 2 per cent sodium thiosulphate were placed in the shower rooms. Care was taken that the children stepped into these before and after their baths. The children were also required to use a dusting powder between their toes containing 2 per cent salicylic acid, 10 per cent kaolin, 10 per cent boric acid; in a base of powdered talc.

The children were again examined after a lapse of one year. In that interval no evidence of activity was noted.

SUMMARY

Examination of 65 children in an orphan's home revealed clinical evidence of ringworm in all.

Positive cultures of *Trichophyton interdigitale* were obtained from 21, or 32 per cent, of the children.

As a diagnostic measure, trichophytin, irrespective of its source, was valueless. It is of interest to note, however, that the incidence of positive reactions increased with the age of the patient. The young children almost invariably gave a negative reaction, although clinical manifestations may have been severe.

Prophylaxis was successful in stamping out active manifestations of the disease.

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Case Reports

METHÆMOGLOBINÆMIA DUE TO SULPHANILAMIDE THERAPY*

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Paton and Eaton[1] have reported the occurrence of methæmoglobinæmia as a result of treatment with sulphanilamide. This fits in with our experiences with oral administration of the drug. The occurrence of this pigment in the blood does not appear to be related to dosage; it was found with relatively small amounts, as well as with large doses. In one of our cases, for example, (female, age 11 years), methæmoglobinæmia, with marked cyanosis, was found after two doses only of 7.5 grains each, and in another case (male, age 22 years), after three doses only of 15 grains each. Paton and Eaton[1] found that the methæmoglobinæmia and the resultant cyanosis usually disappear within 24 to 48 hours after the drug is discontinued. This is also in accord with our experience.

In most of our cases, the methæmoglobinæmia did not appear to influence the progress of the disease for which sulphanilamide was used. Therefore, as far as is known at present, its occurrence is no contraindication for continuing the drug. However, little is known of *all* of its possible toxic effects. *A priori*, if it causes methæmoglobinæmia, it may be expected to have other and more serious effects. Its chemical structure alone suggests other possibilities, particularly those of benzene and aniline poisoning. Actually there have been reported from its use acute hæmolytic anæmia and agranulocytosis.[2] It is thus obvious that special attention should be paid to those cases in which methæmoglobinæmia develops rapidly after relatively small doses.

Although the methæmoglobinæmia, *per se*, is, as a rule, not harmful, it may be under certain conditions, as the following case illustrates. Findings relevant to the methæmoglobinæmia only are reported, and it is not intended that the data should be interpreted as evidence for or against the efficacy of sulphanilamide in the treatment of infection.

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Received for publication June 17, 1937.

REPORT OF CASE

M.M., female, aged 22 years, was admitted to the service of Dr. A. H. Gordon on May 16, 1937 with pneumonia due to *S. hæmolyticus*. She was markedly cyanotic. The first dose of sulphanilamide was given at 2 a.m. May 17th (see Table). On May 19th, it was noticed that, although some of the cyanosis disappeared when she was placed in an oxygen tent, it was still much more marked than would be expected from the lesion in the lung. On the following day (May 20th), as there was no change in the condition, the blood was examined spectroscopically and methæmoglobin was found.* The amount was then estimated quantitatively by determining the difference between the total hæmoglobin by Wu's cyanhæmoglobin method[3] and the oxygen capacity by Van Slyke's method.[4, 5]†

It will be noted that, on the first examination (May 20th), there were 2.5 g. of methæmoglobin per 100 c.c. of blood, that is, this abnormal pigment accounted for 22 per cent of the total hæmoglobin. The total amount of hæmoglobin was only 11.6 g. per 100 c.c. Thus the anoxæmia due to the pneumonia was aggravated not only by anæmia but also by the methæmoglobinæmia, since the latter pigment is unable to carry oxygen; the amount of oxygen-carrying hæmoglobin was 9.1 g. only per 100 c.c. The problem was further complicated by our inability to secure a suitable donor for blood transfusion; the patient belonged to Group II (Moss) but by cross agglutination tests with bloods from donors of Groups II and IV, major agglutination occurred in each case.

In view of the favourable results reported by others with sulphanilamide therapy in hæmolytic streptococcic infections, large dosages of this drug appeared to be indicated, providing they did not lead to further reduction of the amount of hæmoglobin capable of carrying oxygen. Daily estimations were therefore made of (*a*) total hæmoglobin, (*b*) oxygen-carrying hæmoglobin and (*c*) methæmoglobin. The combined data are shown in the accompanying table (see page 64).

It will be noted that except for a slight rise on May 21st, the degree of methæmoglobinæmia did not increase. No sulphates were given by mouth since they may favour formation of sulphæmoglobin. The bloods, however, were also examined spectroscopically for the presence of this pigment.* Its appearance is of clinical importance because of the slow rate of removal of this compound; whereas methæmoglobin disappears rapidly—usually within 24 to 48 hours—after discontinuing sulphanilamide, sulphæmoglobin may persist for as long as six weeks.[1] No sulphæmoglobin was found. Since the degree of methæmoglobinæmia did not increase and there was no formation of sulphæmoglobin, the sulphanilamide was given in large doses until the pneumonia appeared to improve clinically. It will be noted that the methæmoglobin disappeared from the blood 48 hours after the drug had been stopped.

The data of May 20th to May 25th inclusive show that, although the degree of methæmoglobinæmia remained fairly constant, the total and oxygen-carrying hæmoglobin contents of the blood decreased steadily. A further attempt was therefore made to obtain a suitable donor for transfusion. A Group II donor, whose blood showed slight major and no minor agglutination with the patient's blood, was eventually found. On May 25th and 26th, 350 and 150 c.c. of this blood were given respectively, with no unfavourable reactions. It will be noted that the effects of these transfusions were (*a*) cessation of further reduction of the oxygen-carrying hæmoglobin content of the blood and (*b*) an unexpected reduction in the degree of methæmoglobinæmia from 2.1 to 0.6 g. per 100 c.c. with no return to the previously existent level. The total hæmoglobin values suggest that the reduction of the degree of methæmoglobinæmia was not due to reconversion into oxygen-carrying hæmoglobin but to destruction.

The data are also of interest in that they indicate the sensitivity of the spectroscopic method for the detection of methæmoglobin in the blood. A very faint absorption band could be seen in the red region of the spectrum with as little as 0.4 g. of methæmoglobin per 100 c.c. of blood. In another case of methæmoglobinæmia, the characteristic band was seen when the blood contained 0.7 g. The sensitivity of spectroscopic examination, it should be noted, depends upon a number of factors, namely (*a*) type of spectroscope; (*b*) source of illumination; (*c*) visual acuity of the observer; (*d*) dilution of the blood, and (*e*) depth of the layer of solution examined. Bloem,[6] with the use of solutions of methæmoglobin viewed through 1 in 5 dilutions of blood and a depth of one inch, found the limit of the spectroscopic method to be about 0.3 g. per 100 c.c.

SUMMARY

1. Attention is drawn to the occurrence of methæmoglobinæmia due to oral administration of sulphanilamide.

2. Reports of acute hæmolytic anæmia and agranulocytosis following the use of sulphanil-

* The methæmoglobin was identified by the following tests:—The blood was laked with the minimum amount of distilled water which permitted a clear view of the red region of the spectrum. In the first examinations, four volumes of water had to be added to one volume of blood. Later, because of reduction of the hæmoglobin content of the blood, three and then two volumes only of water had to be added to one volume of blood. The laked blood was placed in a tube of 11 mm. diameter and examined with a small hand spectroscope against bright daylight. Proof that the band found in the red region of the spectrum was due to methæmoglobin was established by three tests; the band disappeared immediately on the addition to 3 cc. of laked blood of (*a*) one drop of a 1 per cent aqueous solution of potassium cyanide or (*b*) one drop of Stokes' reagent; finally, the position of the band was not affected by saturation of the blood with carbon monoxide. The methæmoglobin was confined to the corpuscles. Repeated spectroscopic analyses of the plasma showed no methæmoglobin.

† Some of the blood pigment which could not carry oxygen may have been a compound, other than methæmoglobin, which could not be recognized by spectroscopic examination. However, the parallelism between the intensity of the absorption band of methæmoglobin and these quantitative estimations suggests that most, if not all, of the abnormal pigment was methæmoglobin.

* There are numerous reports of sulphæmoglobinæmia following administration of sulphanilamide and its related compounds. This literature has been reviewed by Paton and Eaton.[1] As yet, this condition has not been met with in this clinic.

TABLE

SHOWING DOSAGE OF SULPHANILAMIDE AND RESULTS OF SPECTROSCOPIC ANALYSES AND QUANTITATIVE ESTIMATIONS OF TOTAL HÆMOGLOBIN, OXYGEN-CARRYING HÆMOGLOBIN AND METHÆMOGLOBIN OF BLOOD IN CASE OF HÆMOLYTIC STREPTOCOCCIC PNEUMONIA (Hosp. No. 2734/37)

Date	*Hour*	*Type of hæmoglobin gms. per 100 c.c. blood*			*Intensity of absorption band of met-hæmoglobin*	*Dosage of sulphanilamide (given by mouth)*
		Total	*Oxygen-carrying*	*Methæmo-globin*		
May 16	.....	....	....	....	.....	0
May 17	.....	....	....	....	.....	gr. XV q4h omitting one dose
May 18	.....	....	....	....	.....	" "
May 19	.....	....	....	....	.....	gr. XV q4h
May 20	2.00 p.m.	11.6	9.1	2.5	+	"
May 21	10.00 a.m.	11.7	8.8	2.9	+	"
May 22	9.30 a.m.	10.5	8.6	1.9	+	"
May 23	10.00 a.m.	10.2	8.0	2.2	+	"
May 24	10.30 a.m.	9.9	7.4	2.5	+	"
May 25*	8.15 a.m.	9.9	7.8	2.1	+	"
May 26†	8.15 a.m.	8.9	7.8	1.1	faint	"
May 27	8.15 a.m.	8.6	8.0	0.6	very faint	"
May 28	8.45 a.m.	8.5	7.8	0.7	"	"
May 29	8.15 a.m.	8.3	7.4	0.9	"	"
May 30	12.30 p.m.	9.2	8.1	1.1	faint	gr. XV at 4 a.m. and 8 a.m. only
May 31	11.00 a.m.	8.5	7.6	0.9	very faint	gr. XV q4h starting at 12 noon
June 1	.....	....	....	....	.....	gr. XV q4h
June 2	8.15 a.m.	8.0	7.6	0.4	very faint	gr. XV at 4 a.m. and 8 a.m. only
June 3	1.00 p.m.	7.5	7.1	0.4	negative	0
June 4	8.45 a.m.	7.5	7.4	0	"	0

*Blood transfusion (350 c.c.) at 5 p.m.
†Blood transfusion (150 c.c.) and 175 c.c. 10 per cent glucose in normal saline intravenously at 8 p.m.

amide and the close chemical relationship between this drug and benzene and aniline suggest that search for toxic effects more harmful than methæmoglobinæmia should be a routine.

3. A case of pneumonia due to *S. hæmolyticus* and treated with sulphanilamide is cited as an example of a condition in which methæmoglobinæmia may be harmful.

4. The significance of spectroscopic analyses and quantitative estimations of the different forms of hæmoglobin of the blood is briefly discussed.

5. Data are reported which indicate the sensitivity of the spectroscopic method for the detection of methæmoglobin in blood.

The authors wish to express their thanks to Dr. A. H. Gordon, who supervised the treatment of the above mentioned case of pneumonia, and to members of the staff for the permission granted to one of the writers (E.H.B.) to investigate all of the patients in the hospital who have been treated with sulphanilamide.

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A CASE OF APLASTIC ANÆMIA IN A CHILD

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On account of the comparative rarity of aplastic anæmia and of the length of time that this particular case has been under observation and treatment it may be worthy of report.

The patient was a girl, born November 5, 1928, of perfectly healthy parents. The labour was normal, almost precipitate, and nothing abnormal was noted at birth or during the post-natal hospital period. She was breast-fed for five months and during this time, from the 6th week, she had attacks of eczema. I also noticed that she gradually developed a somewhat yellowish skin, with cold hands and feet and a bluish tint to the lips and finger nails. Thinking the breast milk might be at fault, I tried her with a caloric modification of pasteurized cows' milk, but this disagreed, so from the 6th to the 7th month I gave lactic acid milk. This also was not tolerated, so from the 7th to the 14th month protein milk was given, with moderately good results. From 14 to 20 months "klim" was used, and from 20 to 24 months whole milk. Then from 24 to 30 months various articles of diet were