STOSSTHERAPY IN ACUTE RESPIRATORY INFECTION IN CHILDREN*

BY

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Stosstherapy was the name given by Harnapp (1938) to the method of treatment of rickets with a single massive dose of one million units of vitamin D. Later, Gaisford (1951) used the name to describe the single massive dose of sulphonamide which he used in the treatment of pneumonia and other infections. In Denmark and America this method of treatment has been called "shock dose."

Although stosstherapy is a relatively new method of treatment, Ehrlich (1913) was well aware of the advantages of cure by a massive single dose, the *therapia sterilisans magna*: "We must give strong doses, according to the maxim *Frapper fort et frapper vite*." In fact, Ehrlich had some success with stosstherapy, for a 300-bedded hospital in Surinam, used solely for the treatment of yaws, was emptied.

The first published report of stosstherapy in the treatment of respiratory infection in children was by Platt (1940). He used sulphapyridine in a single dose of 0.3 g. per kg., up to a maximum of 4 g. Patients treated during the same period with multiple doses formed a control group. He reported good and comparable results in the two groups. Since then other reports of satisfactory results from stosstherapy have followed (Karelitz and Weinstein, 1940; Vollmer *et al.*, 1944; Lauria, 1947; Wilken-Jensen, 1948; Friderichsen and Walther, 1950). The last-mentioned authors began using stosstherapy in 1941; from 1944 they used sulphathiazole instead of sulphapyridine, and after 1946 for 39 children they used penicillin in addition to sulphathiazole. By 1949 they had treated 1,500 children by stosstherapy. 875 of their patients had pneumonia, 90 lobar and 785 bronchopneumonia, of which 280 occurred in infants under 1 year of age. The case fatality for the 875 children with pneumonia was 4.9%. Jersild *et al.* (1956) treated 245 children with pneumonia with a single dose of 200,000 to 400,000 units of procaine penicillin, and compared the results with 323 cases of pneumonia treated with injections of procaine penicillin twice daily for five days; the single dose was as effective as the five-day course.

Material and Methods

The object of the present study was to compare the results of stosstherapy in acute lower respiratory infection in children with those of standard continuous chemotherapy. Between October, 1952, and October, 1954, 174 children with acute lower respiratory infection were admitted to the Evelina Children's Hospital of Guy's Hospital, and were treated with penicillin by injection or oral sulphonamide, or a combination of both. Sixty of these were treated by stosstherapy and 114 by a conventional continuous course of chemotherapy.

It was necessary to exclude certain patients from both treatment groups. From the stoss group of 60, 8 children were excluded (2, hilar adenitis; 1, whooping-cough; 1, mongol; 1, staphylococcal pneumonia; 1, middle-lobe collapse; 1, treatment delayed 16 days; 1, bronchiectasis). From the standard group of 114, 60 children were excluded (41, duration of penicillin less than five days; 10, treated with sulphonamide only; 5, chest films mislaid; 1, aged

2 weeks; 1, fibrocystic disease of the pancreas; 1, death within one hour of admission; 1, agammaglobinaemia). After these exclusions there remained for the present study 52 children in the stoss group and 54 in the standard group.

The method of treatment (stoss or standard) to be given was chosen by any one of fourteen doctors who admitted the patients and whose personal preferences dictated his decision.

The grouping of patients who clinically appear to have an acute infection of the lower respiratory tract is not easy, whether aetiological or anatomical classification is attempted. For simplicity in this article, the patients who clinically had an acute infection of the lower respiratory tract were grouped by radiological appearances: group 1a, consolidation confined to bronchopulmonary segments; group 1b, consolidation confined to whole lobe; group 2, consolidation not confined to bronchopulmonary segments, (a) discrete, (b) confluent; group 3, no radiological changes.

Comparability of the Two Treatment Groups.—Table I shows that the two groups on admission were similar in respect of clinical and radiological grouping, age, sex,

TABLE I.—Comparison of Main Features of Stoss and Standard Groups

	Stoss	Standard
Total in group	52	54
Age		
1-12-1 year	11	14
2 years	9	12
4 "	14	12
6 "	11	11
12 "	7	5
Sex:		
Boys	30	31
Girls	22	23
No. severely ill	14	15
Average No. of days ill before admission	3.5	5
Previous history of acute lower respiratory infection	18	11
Immediate previous chemotherapy	4	14
Mean temperature on admission		
Oral	103° F. (39.4° C.)	102.1° F. (38.9° C.)
Rectal	101.7° F. (38.7° C.)	102.7° F. (39.3° C.)
Mean pulse rate on admission	136	132
Mean respiratory rate on admission	39	45
Radiological grouping		
Group 1a	22	22
1b	7	5
2a	7	3
2b	4	4
Mixed 2a and 2b	17	19
3	1	1
White blood count (cells/c.mm.). No. of patients		
Over 20,000	51	46
15,000-20,000	7	3
10,000-15,000	12	8
Under 10,000	14	13
Additional features on admission		
Pleural effusion	18	22
Otitis media	3	4
Tonsillitis	0	1
Anaemia	1	0
	(Hb 8.9 g.% and 7.5 g.%)	(Hb 8.6 g.%)

number severely ill, and mean pulse rate. Patients in the stoss group differed from those in the standard group in the following respects: the average duration of illness before admission was shorter; more had a previous history of acute lower respiratory infection; fewer had been given immediate previous chemotherapy; the mean temperature on admission was higher in those patients in whom the temperature was recorded by the oral route—that is, the older children—and lower in those in whom the temperature was recorded by the rectal route; the mean respiratory rate on admission was lower; the white blood count was higher. Each group also showed small differences by the presence of associated features, such as pleural effusion, otitis media, tonsillitis, and anaemia.

Treatment.—Of 52 stosstherapy children, 48 received both sulphadimidine and penicillin; 4 had penicillin alone. The sulphadimidine was given by mouth. The dose was 0.3 g. per kg. up to a usual maximum of 4 g.; one robust child was given 5 g. The penicillin was given by intramuscular injection. 39 children were given, in addition to sulphadimidine, 0.2 to 0.5 mega unit of sodium penicillin; nine had, in addition to sulphadimidine, 0.3 mega unit of procaine penicillin with 0.1 mega unit of sodium penicillin (= 1 ml. "seclopen"). Three children had only 1 ml. of seclopen; one had only 0.3 mega unit of sodium penicillin. In the standard group, treatment was either with repeated intramuscular injections of

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penicillin or by such penicillin treatment combined with sulphadimidine. Penicillin injections were given six-hourly when the sodium salt was used and once or twice daily when seclopen was used. The dose of sulphadimidine was 0.15 to 0.2 g. per kg. per 24 hours, and this was given six-hourly in divided doses by mouth. Treatment was continued for at least five days.

Results of Treatment

Treatment was considered successful if the initial response was satisfactory and improvement maintained, if treatment did not need to be repeated or changed, and if there were no relapses or complications. Failures were those who did not respond to the initial treatment and who required a change of treatment. Relapses were those who deteriorated after an initial apparently satisfactory response. There was one patient who responded incompletely; this child improved initially, but improvement was not maintained. Table II shows the overall results of treatment.

TABLE II.—Summary of Response to Treatment

	No.	Successes	Failures	Relapses	Complications	Incomplete Response
Stoss	52	43	2	3	3	1
Standard	54	46	4	0	4	0

Failures.—Of the two failures in the stoss group one was subsequently given a course of penicillin and sulphadimidine, failed to respond, and was finally given a course of chlortetracycline with fair results; the other was subsequently given a course of penicillin and sulphadimidine, and responded fairly well. Of the four failures in the standard group, one responded well when sulphadimidine was added to the penicillin already being given, two responded fairly well to the substitution of chlortetracycline, and one failed to respond to chloramphenicol with sulphadimidine but subsequently made a fair response to chlortetracycline. It may be significant that these four patients had normal radiographs.

Relapses.—Of the three relapses in the stoss group, two were given a second stoss dose and one a course of penicillin and sulphadimidine. All three responded well.

Complications.—The complications were all extrapulmonary. The three patients in the stoss group with complications (two with otitis media and one with pharyngitis) responded well to a single further injection of penicillin and the four in the standard group (two with otitis media and two with pharyngitis) to a further course of penicillin.

Further Study of Response to Treatment

This response is considered under the headings of temperature, pulse, respiration, signs in the chest, radiological signs, and length of stay in hospital. The analyses have been confined to the 43 patients in the stoss group and the 46 in the standard group who were classified as successes (Table II).

Temperature

In children under 5 years of age all readings (except in one child in whom readings were axillary) were taken rectally; in children 5 years or over it was taken by mouth. Readings were made every four hours. The exclusions were:

	Stoss	Standard
Exclusions:		
Afebrile on admission	3	6
Delayed treatment	1	0
Axillary readings	0	1
No. analysed	39	39

"Afebrile" includes any patient whose rectal temperature was under 100.2° F. (37.9° C.) or whose oral temperature was under 99.2° F. (37.3° C.). The number remaining for analysis was 39 in each treatment group. The temperatures were rectal readings in 31 and 26 patients in the stoss and standard groups respectively. As there is no agreement on the exact figure which represents a normal temperature, and the site at which the temperature is recorded influences the

reading (Moncrieff and Hussey, 1948), evaluation of response has been based on fulfilment of two criteria:

Criterion I.—The duration of time in hours from the temperature recording just preceding the beginning of treatment to the time when the temperature first touches 100° F. (37.8° C.) or lower in the rectal series, and 99° F. (37.2° C.) or lower in the oral series.

Criterion II.—As for Criterion I, but the temperature must remain at 100° F. (37.8° C.) rectally or lower for a period of at least 24 hours, and 99° F. (37.2° C.) or lower for the oral series.

The fulfilment of criteria I and II for the rectal readings is illustrated in Figs. 1 and 2. It can be seen that there were considerably more which fulfilled criteria I and II

FIG. 1.—Fulfilment of criteria I and II for temperature (rectal).

FIG. 2.—Fulfilment of criteria I and II for temperature (rectal).

earlier in the stoss group. For instance, 52% in the stoss group compared with 16% in the standard group, and 42% compared with 16%, fulfilled criteria I and II respectively within eight hours of treatment. Similar observations were made in the oral series.

In order to exclude the possible relationship of the height of the temperature on admission to the speed with which it responded to treatment, the stoss and standard groups of patients were subdivided into two groups according to whether their temperature on admission was 102.4° F. (39.1° C.) and under, or 102.6° F. (39.2° C.) and over. These two groups were analysed with reference to the speed with which criterion II was fulfilled. For the lower-temperature group, stoss was more efficient than standard in fulfilling criterion II; thus more than 50% of the 23 patients in the

stoss group fulfilled criterion II within eight hours of treatment, compared with 8% of the 13 patients in the standard group. For the higher admission temperature, stoss and standard treatments were about equally effective.

FIG. 3.—Response of temperature.

Temperature Chart for the First Seven Days.—The mean temperature recording for each day was calculated (Fig. 3). The first figure was the first reading taken on admission in the ward. The second figure, day 1, was the mean of the readings taken on the day of admission. On each full day the temperature shown in Fig. 3 was the mean of five readings for each child. For instance, the figure for day 2 was the mean of 285 readings by the rectal route for both treatment groups. It can be seen that the curves in the rectal and oral series were very similar.

Pulse Rate

The exclusions from the analysis of the pulse rate were:

Exclusions:	Stoss	Standard
Delayed treatment	1	0
Notes mislaid	1	0
No. analysed	41	46

FIG. 4.—Response of the pulse rate.

The mean pulse rate on admission was 136 in the stoss group and 132 in the standard group. There were a greater number of stoss cases with very high pulse rates—for example, 7% of the patients analysed in the stoss group had pulse rates over 160 a minute, compared with none in the standard group.

Fig. 4 shows the curve for each treatment group; the response was very similar, but there was a sharper initial drop in the stoss group in spite of a slightly higher rate on admission.

Respiratory Rate

The exclusions from the analysis of the respiratory rate were the same as for the pulse rate. The mean respiratory

rate on admission was 39 in the stoss group and 45 in the standard group. Although the mean rate was higher in the standard group, there were a greater number of patients in the stoss group who on admission had a very high respiratory rate (76 to 85 per minute). Fig. 5 shows the course of the respiratory rate over the first seven days. The two curves were very similar.

Rise of Temperature, Pulse Rate, and Respiratory Rate After Admission

The temperatures and pulse and respiratory rates of many of the children rose after admission, although treatment had already been started. The initial ward readings, taken on admission, were therefore compared with the highest readings above these values in the first 24 hours. The average rise in the stoss and standard groups was thus calculated. Table III and Fig. 6 show the incidence and extent of

this rise of temperature and of pulse and respiratory rates which occurred within the first 24 hours of admission. The difference in the numbers analysed for temperature can be accounted for by the inclusion of three and six patients in the stoss and standard groups respectively who were afebrile on admission, and the exclusion of one patient in the stoss group whose records were mislaid.

FIG. 5.—Response of the respiratory rate.

FIG. 6.—The lower figure shows the incidence of rise of temperature, pulse, and respiration above that on admission within 24 hours following treatment. The upper figure shows the magnitude of this rise.

TABLE III.—Incidence of Magnitude of Rise of Temperature, Pulse and Respiratory Rates Within 24 Hours Following Treatment

	Temperature	Pulse	Respiration
<i>Incidence</i>			
Stoss	7 (17½%)	20 (49%)	25 (61%)
Standard	14 (31½%)	25 (54%)	27 (58%)
<i>Magnitude</i>			
Stoss	0.8° F.	13	9
Standard	1.4° F.	16	13

The greatest difference between the two treatment groups was in respect of the temperature rise. A rise of temperature after admission occurred nearly twice as often in the standard group as in the stoss group, and this rise was also nearly twice as great. The differences for rise in pulse and respiratory rates were smaller, but nevertheless showed the same trend.

Physical Signs in Chest

After exclusion of patients who on admission had no physical signs in the chest there remained 39 and 44 in the stoss and standard groups respectively. Signs in the chest were recorded on alternate days or more frequently.

Fig. 7 shows the day on which signs in the chest cleared. The mean time for each group to clear was 6.3 and 8.3 days for stoss and standard respectively. By the end of one week 28 (72%) of the stoss group compared with 20 (46%) of the standard group, and by the tenth day 37 (95%) compared with 31 (71%) respectively, had clear chests. The number of days before 50% of patients were free of chest signs was 5½ in the stoss and 8½ in the standard groups.

FIG. 7.—Rate of disappearance of physical signs in chest.

Clearing of Radiographs

The average time at which the chest film had returned to normal was difficult to assess because some patients failed to attend for follow-up at the appointed time; in some of these a radiograph was finally taken some weeks later, and therefore the earliest time for the chest radiograph to have returned to normal may have been missed.

After exclusion of those who had radiographs taken at more than fortnightly intervals, and of those whose radiographs were normal on admission, there remained 12 in the stoss group and 13 in the standard group. Table IV shows the results, which did not reveal any substantial difference between the two treatment groups.

TABLE IV.—Average Time of Return of Radiograph to Normal

	No.	Weeks						
		1	2	3	4	5	6	Over 6
Stoss	12	3	4	4	0	1	0	0
Standard	13	2	5	4	1	1	0	0

Length of Stay in Hospital

The length of stay in hospital has been analysed, although it was realized that there were many variable factors which influenced it, such as home conditions and the individual preference of the physician. In the stoss group 42, and in the standard group 46, patients remained for analysis after exclusion of one in the stoss group in whom treatment had been delayed. Fig. 8 shows the percentage of patients who were discharged each day. By the 10th day 21 patients (50%) in the stoss group and 14 (30%) in the standard group had been discharged from hospital. The mean day of discharge was 12.3 in the stoss group and 13.1 in the standard group.

FIG. 8.—Length of stay. Percentage of patients discharged each day.

Secondary Fever

A secondary rise of temperature occurring between three and seven days after starting treatment was observed in many patients of both groups. In the present series it has been recorded if the rectal temperature rose to 100.2° F. (37.9° C.) and over, or the oral to 99.2° F. (37.3° C.) and over within seven days of admission, provided the temperature had been below these levels for 24 hours or more. The incidence and the highest readings in patients who had secondary fever are shown in Table V.

This secondary rise of fever occurred in 10 children (23 readings) in the stoss group of 41 patients and in 8 children

TABLE V.—Maximum Readings (°F.) in Patients with Secondary Fever

	Total	No.	99.2-100	100.2-101	101.2-102	102.2-103
Stoss	33 (rectal)	7	0	4	2	1
	8 (oral)	3	3	0	0	0
Standard	32 (rectal)	4	0	4	0	0
	13 (oral)	4	3	1	0	0

FIG. 9.—Case 61 on admission. Left upper lobe consolidation.

(12 readings) in the standard group of 45 patients. The most common day on which secondary fever occurred was the fifth (in four patients) following stosstherapy, and the sixth (in four patients) following standard therapy. Secondary fever after stosstherapy has been recognized by previous observers (Platt, 1940; Minetto, 1944; Lauria, 1947; Wilken-Jensen, 1948), but no satisfactory explanation for its occurrence has been offered. In Platt's series, 14 of his 41 patients developed a secondary rise of fever on day 2 or 3, and two others on day 6. It was surprising to find that this rise occurred in as many as 18% following standard therapy. It is important to know that this secondary rise of fever occurs in about one in three or four patients following stosstherapy, for by itself it is not an indication for further treatment.

Illustrative Cases

Typical Response. *Case 61.*—A girl aged 7½ years was admitted to hospital twelve hours after the onset of vomiting and pain in the left side of her chest. She was ill, and had

FIG. 10.—Progress of Case 61 treated by stosstherapy.

FIG. 11.—Case 61, 13 days after treatment; pleural thickening oblique fissure.

signs of consolidation over the left upper zone (Fig. 9); neck stiffness and Kernig's sign were also present. She was treated with sulphadimidine, 4 g. by mouth, and 500,000 units of sodium penicillin by intramuscular injection. Her subsequent clinical and radiological progress is shown in Figs. 10 and 11. On the next day she was better in all respects. She continued to make good progress; by the seventh day no signs were present in the chest, and she was getting up. By the thirteenth day her chest was almost normal radiologically (Fig. 11). She was discharged home on the fourteenth day, having gained 3 lb. (1.4 kg.) in weight.

Relapse. *Case 48.*—An ill boy aged 5½ years was admitted to hospital with a right lower lobe pneumonia (Figs. 12 and 13). He responded well to stosstherapy, but on the ninth day relapse occurred and he was given a second stoss dose of 3.5 g. of sulphadimidine and 500,000 units of sodium penicillin, to which he responded well. Secondary fever occurred three days after this second dose (shown as 12th day in Fig. 12).

Discussion

In the treatment of acute respiratory infections with sulphonamide and penicillin little attention has been given to consideration of the minimum duration of chemotherapy necessary. The concept that a certain blood level of sulphonamide or penicillin should be maintained for several days has dominated both dosage and the duration of treatment. A specified number of days of treatment (Medical Research Council, 1943), a specified total amount of drug, or a certain duration after the patient has become apyrexial have been some of the recommendations made. Hawking and Lawrence (1950) advised continuing the drug until the time the crisis would have occurred. As early as 1938, however, Whitby (1938), in referring to the sulphonamides, said, "Dosage and the duration of the course provide ample opportunity for the art of medicine where experience and judgment will give the best results." Experimentally and clinically it is clear that what these drugs are going to accomplish they do quickly; there is no justification for giving a prolonged course."

In reviewing the dosage of penicillin in bacterial infections, Marshall (1948) pointed out that, although it is established with certainty that the administration of adequate amounts of penicillin by a dosage schedule which maintains a more or less constant concentration of drug in the blood for a certain time will cure many severe infections, it is by no means established that this dosage schedule is the most satisfactory or the only one which is effective. He goes on to say that dosage has been based on two unproved assumptions: firstly, that it is necessary to maintain constant blood levels; and, secondly, that observations *in vitro* can be transposed without modification to human disease. Some writers, discarding the theory of constant blood levels, have recommended intermittent treatment (Bigger, 1944a, 1944b; Tumulty and Zubrod, 1948; Price *et al.*, 1949; Hamburger *et al.*, 1949). In the present series, constant blood levels were unnecessary, for results as good as those on standard treatment were obtained with stosstherapy; indeed, stosstherapy is the exact antithesis of the theory of constant blood levels. It is necessary to emphasize that, although a single dose will be sufficient in most patients, stosstherapy does not necessarily confine itself to a single dose, for an essential feature of stosstherapy is that treatment is kept under review and is guided by clinical considerations. The patient's response is reviewed at intervals of 12 to 18 hours during the first 36 hours, so that if the response has been inadequate a second stoss dose can be given or chemotherapy changed.

The results of the present investigation have shown that in acute respiratory infection in children stosstherapy produced as good results as standard treatment. A slightly but not significantly higher relapse rate occurred, but response to further stoss or standard therapy was excellent. When a more detailed analysis of the response to treatment was

made, stosstherapy was again as good as standard. In most instances the figures in the stoss group, especially those of temperature response, were better than those in the standard group. A rise of temperature, pulse rate, and respiratory rate within 24 hours after the start of treatment commonly occurred in both treatment groups, but the incidence and magnitude of the temperature rise was much less than in the stoss group.

Advantages of Stosstherapy

Many of the side-effects of the sulphonamides, such as nausea, anorexia, drug fever, leucopenia, rashes, mental changes, and haematuria, are related to the total amount of drug taken and the duration of treatment; these side-effects, therefore, are rarely seen in stosstherapy. In the present series no such effects were seen and there were no cases of macroscopic haematuria; microscopical examination of the urine was not done routinely following stosstherapy, but no excess red cells were present in the urine of the few patients so examined. Penicillin also has side-effects, and some of the reactions are related to the duration of treatment (Lawrence *et al.*, 1953). A single injection is therefore less likely to cause these side-effects than multiple injections.

One injection compared with twenty or more is a big advantage, especially in children; pain and the fear of the next "prick" do not occur. As only a few patients need further treatment, overtreatment of many patients is avoided. Patients have less need to be admitted to hospital. All the hazards associated with injections are reduced to a minimum. From the nurses' point of view more time is available for nursing.

Repeated doses or, worse, injections disturb the patient's rest and sleep; this is particularly objectionable in ill patients during the first few days, when adequate sleep and rest are so essential. Although the newer sulphonamides cause less anorexia and nausea, some patients still experience these unpleasant side-effects. With one dose, however, nausea and anorexia do not persist for long, and the patient is able to enjoy his food sooner.

The time and labour saved by avoiding repeated doses and injections are considerable. Much time and labour are also saved in the preparation and sterilization of needles and syringes. Fewer syringes are broken. The actual expense of the drugs is also less. In 1953, when this investigation was done, stosstherapy for 50 patients cost about £3 10s. compared with £18 10s. for standard treatment; if stosstherapy were used for all cases the saving would amount to a considerable sum in view of the frequency of respiratory infection.

A more rapid response of the temperature was observed in the stoss group; this has been observed by others (Jersild *et al.*, 1956). Stosstherapy gives an earlier indication of whether the patient is failing to respond to treatment, and a quicker change can be made to different chemotherapy.

A possible objection to stosstherapy is that a large dose of sulphonamide might cause obstruction in the urinary tract. This did not occur in over 1,500 patients treated by

FIG. 13.—Case 48. Right lower lobe consolidation with effusion.

FIG. 12.—Case 48. Good initial response to stosstherapy; relapse occurred on 9th day; responded well to further stoss dose. Secondary rise of fever on 12th day.

stosstherapy so far reported. With the newer more soluble sulphonamides such as sulphadimidine, this danger is a remote one.

The general management of patients treated by stosstherapy is no different from that of patients treated by standard methods; but with stosstherapy the patient and his disease are treated rather than the disease alone. Friderichsen and Walther (1950) have pointed out that clinicians do not feel tempted to give up a certain form of treatment while good results have been so obtained. I hope, however, by having illustrated the advantages of this successful method of chemotherapy, that more will use it. I am sure that those who do so will find the change justified.

Summary

Fifty-two children with acute lower respiratory infection were treated with stosstherapy, a single massive combined dose of sodium penicillin by injection and sulphadimidine by mouth or with penicillin alone, and their response was compared with that of 54 similarly affected children treated by repeated chemotherapy given for five days or more.

The analysis of the cases was based on the overall results (successes, failure, relapses, and complications); and on the response of pyrexia, pulse, and respiratory rates; rate of disappearance of physical and radiological signs; and length of stay in hospital. The analysis showed that those children treated by stosstherapy responded at least as well as those treated by repeated chemotherapy.

The appearance of fever, most commonly occurring between the third and sixth days after both stosstherapy and standard chemotherapy, is described.

It is suggested that, as equally good results are obtained with stosstherapy, its many advantages imply that it should be the method of choice for acute infections of the lower respiratory tract in children.

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MEASUREMENT OF RED-CELL LOSS FROM GASTRO-INTESTINAL TRACT, USING RADIOACTIVE CHROMIUM

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When ^{51}Cr -labelled red cells are introduced into the stomach or duodenum, more than 90% of the chromium can be recovered in the faeces (Owen *et al.*, 1954; Roche *et al.*, 1957). This is not altogether surprising, since chromic oxide is virtually unabsorbed by the gastro-intestinal tract, and has been used as an index material in digestion studies in animals and in man (Hamilton *et al.*, 1928; Kreula, 1947). Roche *et al.* (1957) used the technique of injecting ^{51}Cr -labelled red cells intravenously and then estimating ^{51}Cr loss in the stools to determine the extent of red-cell loss into the gastro-intestinal tract in hookworm disease.

In the present investigation six anaemic patients who were known to be losing red cells in their stools were studied. After the intravenous injection of ^{51}Cr -labelled red cells, the loss of ^{51}Cr in the stools was estimated, and these estimates were used to correct the ^{51}Cr -survival curves. It was thus possible to discover whether or not the blood loss in the stools accounted for the diminished survival of red cells in the circulation.

Methods

Labelling of Red Cells with ^{51}Cr .—Red cells were labelled with approximately 100 μC of ^{51}Cr by the method of Mollison and Veall (1955), using ^{51}Cr with a specific activity of 10–30 μC per μg . of chromium.

Estimation of ^{51}Cr Content of Stools.—Two methods were used. *Method 1:* Daily collections of stools were made in tins (diameter, 12.5 cm.; length, 16.5 cm.), except in patient G.B., from whom collections every three to four days were made. The radioactivity in each tin was measured in a ring counter containing 32 Geiger-Müller tubes, as described by Booth and Mollin (1956). A known aliquot of the injected dose of ^{51}Cr was mixed with 100 g. of sugar and estimated at the same time, as a standard. *Method 2:* Water was added to the faeces, which were then weighed and homogenized. The radioactive content of a 10-ml. aliquot was estimated in a pillar-type scintillation counter. As a standard a similar volume of a 1 in 100 dilution of the injection suspension of red cells was used. The ^{51}Cr content of the stools on any day was expressed as a percentage of the injected ^{51}Cr .

Accuracy of Method 1.—The Geiger-Müller ring counter had a background count of 220 c.p.m., and 1 μC present in the tin gave approximately 130 c.p.m. Thus, with 20 minutes' counting of the background alone and 20 minutes with the source, 1 μC of ^{51}Cr could be estimated with a coefficient of variation of 4%. If 100 μC of ^{51}Cr was injected, and the subject's red-cell volume was 2 litres, then this quantity of ^{51}Cr would represent 20 ml. of red cells. The presence of 0.1 μC of ^{51}Cr , representing 2 ml. of cells, could just be detected if the background counts alone and the background counts together with the ^{51}Cr source were each counted for one hour.

Accuracy of Method 2.—A concentration of 1 μC in 100 ml. gave 1,200 c.p.m. in the scintillation counter and the background counts were of the order of 40 c.p.m. 2,500 counts were usually made, and the coefficient of variation was 2%. A concentration of 0.004 μC per 100 ml. could