The results of early trials with chloramphenicol (Rogers, Koegler, and Gerrard, 1949) suggest that it is an effective therapeutic agent in gastroenteritis. If its value is confirmed the use of streptomycin will be entirely superseded.

Summary

Trials of oral streptomycin for infants under 1 year suffering from endemic non-specific gastroenteritis extended in three stages over the period August, 1947, to February, 1950. The main stage of the investigation included 97 babies who were grouped according to age and to the severity of their disease, and alternate cases in each age group were allocated to the trial and control series.

No clear-cut response to streptomycin has been demonstrated, but the data on which clinical assessment was based show that there was slightly better progress among the streptomycin-treated cases and that the contrast was more marked among the severe cases. Many cases failed to respond to streptomycin, and it cannot be regarded as an effective therapeutic agent for the disease.

Bacteriological studies were made, but the results throw no light on the aetiology of gastroenteritis. Streptomycin in the dosage employed failed to eliminate the special type *Bact. coli*, alpha and beta.

We are grateful to Dr. R. H. Dobbs and Dr. I. M. Anderson for permission to study their cases and for their advice in the planning of the investigations. We are indebted to Dr. B. Levin for his help throughout the investigation and for the provision of the bacteriological data. We also wish to thank Mr. G. Hunt for his technical assistance in the bacteriological studies. Dr. Richard Doll has been kind enough to advise us about the statistical significance of the data.

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Sir John Cockcroft said recently at Oxford that there are three scientific freedoms: freedom to work on any subject in science; freedom to publish results; and freedom to meet other scientists and discuss one's work fully with them. In this country, so far as the first is concerned, while university expenditure is more and more provided by Government funds, the money is administered by the University Grants Committee under a system which leaves them completely free to decide how they will spend it. The only exceptions are the large expenditures on research in nuclear physics and a few other special projects financed by the Department of Scientific and Industrial Research on the recommendation of expert committees. Outside the universities, in research conducted by the Medical Research Council or the Ministry of Supply, for example, a much greater element of planning is evident, because these departments have to work towards certain objectives, but even so probably 30%–50% of the work of the civil departments could be classed as fundamental and long-range research, and therefore not plannable. On the whole, therefore, Sir John thought that scientific freedom in this country is not imperilled by State planning. The second freedom, that of publication, is always subject to one important qualification —that results must not be published unless the worker is as sure of them as is reasonably possible. Secrecy has been retained to-day only in matters of technological importance, which hardly constitutes a restriction on freedom of science. In the Western world there are still fairly complete freedom of movement and a plethora of scientific conferences. But there are signs that this freedom may be subject to some restriction in the future, partly as a result of the passage in the United States of the Internal Security Act.

ON CHEMICAL TESTS FOR BLOOD IN URINE

BY

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Chemical tests for haematuria are still used when a centrifuge and microscope are not available. Little information on their sensitivity is to be found. We therefore report on the absolute and relative sensitivity of the *ortho*tolidine hydrochloride, benzidine, Kastle–Meyer or reduced phenolphthalein, amidopyrine, and guaiac chemical tests, of direct spectroscopy, and of microscopy under standard conditions, and comment on their convenience and reliability.

Experimental

Urine.—The urine samples were prepared from blood (Hb, 14.3 g. per 100 ml., red cells, 5,000,000 per c.mm.) diluted with urine obtained from the same individual. Dilutions were made with fresh urine, urine which had stood for 24 hours to allow oxidation of ascorbic acid, and the same two urines to which had been added 2 mg. of ascorbic acid per 100 ml. This was done because Kohn and Watrous (1938), Barach and Pennock (1943), and Zwarenstein (1949) have found that an excess of ascorbic acid inhibits the benzidine and *o*-tolidine hydrochloride tests; and 2 mg. per 100 ml. represents an average normal concentration. It was found that fresh and stale urines gave the same results, but that ascorbic acid decreased the sensitivity of some tests. The sensitivity varied less than twofold among five replicate experiments.

Technique of Tests.—Most tests were performed as described by Harrison (1947), the *o*-tolidine hydrochloride test as described by Zwarenstein. Spectroscopy consisted in examining a 1-in. (2.5-cm.) layer for the bands of oxyhaemoglobin; it could be made about five times more sensitive by converting the haemoglobin to pyridine haemochromogen, and observing a 2-in. (5-cm.) layer, but this is not a suitable procedure for domiciliary work because of the smell. The centrifuged deposit was obtained by centrifuging 5 ml. at 3,000 rev./min., removing 4 ml. of supernatant, mixing the residue, and examining between slide and cover-slip or in a Fuchs–Rosenthal haemocytometer. The use of the haemocytometer renders the test ten times more sensitive. The sensitivity could be increased about five times more if the Addis technique (12.5 ml. at 3,000 rev./min.; remove 12 ml. and suspend in the residual 0.5 ml.) were used.

Two tests are noteworthy: one comparatively insensitive but simple, the other very sensitive and fairly simple; they are therefore described in detail.

Amidopyrine Test.—Reagents: 5% amidopyrine in 95% alcohol; 10-volume hydrogen peroxide. Acidify 3 ml. of urine with a few drops of acetic acid and overlay with 1–2 ml. of amidopyrine solution; allow 5 to 6 drops of hydrogen peroxide to fall through the alcoholic layer. Stand for a few minutes. A blue or lilac-coloured ring is a positive reaction.

Orthotolidine Hydrochloride Test (Zwarenstein).—Reagents: solid *o*-tolidine hydrochloride; a mixture of equal

volumes of glacial acetic acid and 10-volume hydrogen peroxide (acid peroxide reagent), which keeps for three months. Wash a white porcelain "spot-test" tile with cavities, rinse with 95% spirit, and allow to dry. Do not dry with a cloth, for fragments of fibre may give false positives. Place a "small knife-point"—about 3 mg. or the volume of a grain of rice—of *o*-tolidine hydrochloride in a cavity; add one drop of urine. Stir with a clean glass rod and add one drop of "acid peroxide." A positive reaction appears as a blue coloration, or spreading blue-green streaks which fade after 5–30 minutes to brown. A negative reaction is pale brown.

Results

The results are shown in the Table. Column A gives the number of cells per ml. which can be detected by the techniques described; column B the corresponding concentration of haemoglobin in mg. per 100 ml. of urine;

Method	A	B	C	D
Microscopical*	5×10^3	0·015	100	Nil
o-Tolidine	5×10^4	0·15	10	Nil
Benzidine	5×10^5	1·5	1	4
Kastle-Meyer	5×10^5	1·5	1	Nil
Amidopyrine	10^6	3·0	0·5	2·5
Guaiac	$2·5\times10^6$	7·0	0·2	5
Spectroscopy*	$2·5\times10^6$	7·0	0·2	Nil

* The sensitivity of both these methods can be increased at least fivefold, as described above under "Technique."

column C the relative sensitivities as percentages of that of the centrifuged deposit; and column D the inhibition caused by ascorbic acid (lowest positive concentration without ascorbic acid divided by lowest positive concentration with ascorbic acid).

Technical Difficulties

In the presence of pus all these tests give false positives, which are prevented by boiling the urine; but this treatment reduces sensitivity at least tenfold. All except the Kastle–Meyer give false positives with iodides, and the *o*-tolidine with bromides.

Guaiac.—The tincture of guaiacum resin must be made up weekly, for its sensitivity diminishes on keeping. Some workers prepare an approximately 2% alcoholic solution of the resin at the time of testing. The tubes used are difficult to clean, and if not quite clean give false positives.

Amidopyrine.—The reagent is stable. Tubes are easy to clean and few false positives develop.

Kastle–Meyer, or Reduced Phenolphthalein.—The reagent is troublesome to prepare, but can be bought from B.D.H. at a cost of less than 1d. a test. It deteriorates little on keeping if a little zinc dust is added, but such solutions may require filtration through a hardened filter paper (Whatman 5, 50, or 54) before use. False positives are few. Ascorbic acid does not reduce the sensitivity.

Benzidine.—The reagent must be made up at the time of use from benzidine, glacial acetic acid, and hydrogen peroxide. False positives occur even when tubes appear to be clean. Ascorbic acid reduces the sensitivity about four times.

Orthotolidine Hydrochloride.—The reagents are stable for at least three months. The test is the most sensitive of all and gives few false positives. Ascorbic acid in the concentration used did not reduce the sensitivity.

Conclusion

No single test can be ideal under all conditions. Microscopy of the centrifugal deposit is at least 500 times more sensitive than the guaiac test, and if the Addis procedure be used the ratio reaches 2,500.

For domiciliary work, and as a ward test, the *o*-tolidine hydrochloride test is convenient, very sensitive, and cheap. The porcelain plate can be replaced by a cavity slide 3 by 1 in. (7.5 by 2.5 cm.) to make it more portable. Although in our hands it is much less sensitive for detecting red cells than was claimed by Zwarenstein, it is still ten times more sensitive than any other chemical test, and rarely gives false positives.

The other tests are much less sensitive. The Kastle–Meyer test is very reliable, but the caustic nature of the reagent makes it unsuitable for domiciliary practice. The guaiac test is expensive, insensitive, and not very reliable; it should be abandoned. Should a test of comparable sensitivity be needed, the amidopyrine test is suitable.

In the laboratory it is preferable to examine a centrifuged deposit. If information on the degree and persistence of haematuria alone is needed, then it is justifiable to examine a 1 in. (2.5 cm.) layer of urine with the hand spectroscope; if positive, haemoglobin equivalent to about 2,500,000 red cells per ml. is present; and if negative, then the deposit from 12.5 ml. of urine should be suspended in 0.5 ml. and examined in a Fuchs–Rosenthal chamber.

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GLANDULAR FEVER WITH NEUROLOGICAL COMPLICATIONS

BY

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Epstein and Dameshek (1931) are usually credited with the first description of involvement of the central nervous system in glandular fever (infectious mononucleosis), though Longcope (1922) and Glanzmann (1930) had suspected the association.

I have been able to find only 24 cases of glandular fever, confirmed by a positive Paul–Bunnell test and involving the nervous system, in the literature since 1931 (Sucher and Schwarz, 1936; Gsell, 1937; Pietzonka, 1939; Thomsen and Vimtrup, 1939; Marshall, 1939; Thelander and Shaw, 1941; Landes *et al.*, 1941; Richardson, 1942; Zohman and Silverman, 1942; Hiller and Fox, 1943; Coogan *et al.*, 1945; Ricker *et al.*, 1947; Field, 1948; Bercel, 1948). However, several cases of neurological involvement in clinical glandular fever with a suggestive blood picture but without a positive Paul–Bunnell test have been reported, the most recent being that by Klǿvstad (1950); and several cases of proved glandular fever without clinical involvement of