Treatment

Gastrostomies have been performed repeatedly; but, unless the cardiac end of the stomach is tied, the food flows backwards up the oesophagus into the trachea, except in the very few cases where there is no tracheo-oesophageal fistula. It has been the hope of some surgeons to keep the patients alive long enough to perform an intrathoracic plastic operation at a later date. This seems a forlorn hope, and it is questionable whether it would be justified even if successful, for so many cases are associated with multiple congenital lesions.

Summary

1. A report of a case of congenital atresia of the oesophagus with tracheo-oesophageal fistula is given.
2. The indications are that the anomaly occurs much more often than is generally believed.
3. The anomaly is nearly always associated with other congenital lesions.
4. It produces a quite characteristic syndrome, which if kept in mind makes a clinical diagnosis relatively simple.
5. Auxiliary methods of diagnosis are mentioned.
6. Death has occurred within four weeks in every recorded case.

I should like to express my thanks to Dr. T. F. McNair Scott, recently paediatrician to St. George's Hospital, for allowing me to record this case.

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THE BACTERIOSTATIC EFFECTS OF SULPHONAMIDE-P, SOLUSEPTASINE, AND M & B 693

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The bacteriostatic properties of these three drugs on *Streptococcus viridans* and *Staphylococcus aureus* were examined by the slide method of Wright, modified by Fleming (1924, 1938). A different technique, described below, was necessary in the cases of *Neisseria gonorrhoeae* and *N. meningitidis*, as these organisms did not show sufficiently differentiated colonies for counting. The drugs were dissolved in saline and kept made up in dilutions of 1 in 1,000, sterilized by heating to 60° C. for one-half to one hour.

Streptococcus viridans and *Staphylococcus aureus*

TECHNIQUE

The tests were set up in the following manner. First a suspension of a fresh culture of the organism in sterile saline was prepared and matched to correspond in density with Brown's No. 1 tube. Human blood was then withdrawn and defibrinated by shaking with glass beads. Half

of the blood was separated and forced five to seven times through cotton-wool to reduce the number of leucocytes present. In this way the white cell count was lowered to 500 to 1,000 per c.mm. and most of the polymorphs were removed. Blood so treated is referred to below as "deleucocyted." Defibrinated blood was found to be slightly deleucocyted, the white cell count after defibrination falling from about 7,000 to 5,000 per c.mm., but many polymorphonuclear cells were still present.

Mixtures were then made of one volume of suspension of the organisms to three volumes of defibrinated and of deleucocyted blood. Equal volumes of the blood-organism mixtures and the dilution of the antiseptic were then mixed and slides set up as described by Fleming. Three dilutions of each chemical substance were employed, and the final dilutions in the compartments of the slides were 1 in 2,000, 1 in 20,000, and 1 in 60,000. Prepared slides were incubated at 37° C. in moist conditions for twenty-four hours, and after incubation colonies were counted under the low power of a microscope.

RESULTS

Streptococcus viridans.—Three strains isolated from patients' throats were examined, and the results in all three examinations showed that the drugs affected the growth of the organisms, but only in the presence of white blood corpuscles, including polymorphs. A typical result of a count of *Str. viridans* is shown in Table I.

TABLE I.—Effect of Drugs on *Str. viridans*

Drug	Number of Colonies in Dilutions of—			Control
	1/2,000	1/20,000	1/60,000	
M & B 693 :				
a	16	20	20	900 +
b	Uncountable in all dilutions			+++
Sulphonamide-P :				
a	30	600	900 +	900 +
b	Uncountable in all dilutions			+++
Soluseptasine :				
a	20	800 +	800 +	900 +
b	Uncountable in all dilutions			

a = mixed with defibrinated blood; b = mixed with deleucocyted blood.

+ sign after a number indicates the presence of very small colonies not counted in the figure quoted.

Similar results were obtained for the other strains of *Str. viridans*. In the presence of defibrinated blood containing normal numbers of white cells it will be seen that M & B 693 is a very efficient bacteriostatic agent, even at a dilution of 1 in 60,000, whereas the other two drugs are efficient at a dilution not greater than 1 in 2,000. In deleucocyted blood none of the drugs has much bacteriostatic effect, although the colonies appear much smaller in the high concentrations than in the controls, which contained no drugs.

Staphylococcus aureus.—None of the drugs appeared to have the slightest effect on the growth of this organism. Two strains of staphylococcus, one freshly isolated from a boil, were examined, and in both cases the growth after twenty-four hours was confluent and general in all slides.

Neisseria gonorrhoeae and *N. meningitidis*

TECHNIQUE

These organisms were examined by the slide method, but this was abandoned after a few experiments, as colony formation was poor, making counting very difficult. The following method was then devised. Mixtures of one volume of suspensions of fresh cultures of the organisms and three volumes of defibrinated and deleucocyted blood

respectively were prepared as before. Fifteen drops of these mixtures were then measured into sterile dwarf test-tubes, and equal volumes of the various dilutions of the drugs were added. The final dilutions of the drugs were the same as in the slide technique. The mixtures were shaken and incubated at 37° C. for twenty-four hours under moist conditions. After incubation samples of the contents of the tubes were plated out on blood agar and the plates were incubated for a further twenty-four hours in a moist chamber. The number of colonies on each plate was then counted, and in this way an estimate of the bacteriostatic effects of the dilutions of the drugs was obtained. Table II illustrates a typical result with a stock culture of *N. gonorrhoeae*.

TABLE II.—Effect of Drugs on *N. gonorrhoeae*

Drug	Number of Colonies in Dilutions of—			Control
	1/2,000	1/20,000	1/60,000	
M & B 693 :				
a	0	0	10	77
b	73	80	32	26+
Sulphonamide-P :				
a	6	17	5	77
b	7	9	29	26+
Soluseptasine :				
a	0	2	11	77
b	1	3	3	26+

Here again two of the drugs acted much better in the presence of a full complement of leucocytes. Thus M & B 693 was bacteriostatic at a dilution of 1 in 60,000 in the presence of defibrinated blood, whereas when mixed with de-leucocytised blood it did not appear to be bacteriostatic at a dilution of 1 in 2,000. Sulphonamide-P (sulphanilamide) was bacteriostatic at 1 in 60,000 in the presence of defibrinated blood, but was not active at this dilution when mixed with de-leucocytised blood. This activity of sulphonamide-P is in agreement with the clinical findings of Cokkinis and McElligott (1938). Soluseptasine was active at all dilutions in both defibrinated and de-leucocytised blood. In this case it is possible that some difference in activity might manifest itself at higher dilutions of the drug.

Neisseria meningitidis

Preliminary experiments with a number of different strains of *N. meningitidis* indicated that soluseptasine was not as effective an agent against this organism as was M & B 693. Thus, in mixtures containing normal cerebrospinal fluid, a suspension of an organism grown from a fatal case in a recent epidemic, and various dilutions of the drugs, soluseptasine was found to be bacteriostatic at a dilution of 1 in 1,000 and not at 1 in 10,000, whereas M & B 693 was effective at a dilution as high as 1 in 50,000, even in the absence of blood.

When the organisms were examined by the method described above these results were confirmed, as may be seen in Table III.

The results shown in Table III indicate that in high dilutions the drugs act better in the presence of leucocytes—that is, in defibrinated blood. In lower dilutions sulphonamide-P appears to work slightly better in the absence of the leucocytes. This, however, was not a constant finding.

Of the three drugs M & B 693 appears to inhibit growth slightly more successfully than the other two in all dilutions, and with or without leucocytes. Sulphonamide-P is also effective in high dilution even in the absence of

leucocytes. It should be noted here that our results with this drug are better than those obtained by other authors

TABLE III.—Effect of Drugs on *N. meningitidis*

Drug	Number of Colonies in Dilutions of—			Control
	1/2,000	1/20,000	1/60,000	
M & B 693 :				
a	13	23	11	Confluent
b	0	20 (inf.)	80+	"
Sulphonamide-P :				
a	170	134	54	"
b	23	60	105	"
Soluseptasine :				
a	77	74	300+	"
b	44	700+	confluent	"

"Inf." means that the plate was slightly infected.

(Branham, 1937; Neter, 1938). Soluseptasine has the least effect on the growth of the organisms, although it is active at a dilution of 1 in 20,000 in defibrinated blood.

Summary

The bacteriostatic effects of sulphonamide-P, soluseptasine, and M & B 693 have been examined.

All three drugs inhibit the growth of *Str. viridans* at a dilution of 1 in 2,000 in the presence of defibrinated human blood, M & B 693 doing so at a dilution as high as 1 in 10,000. None of these drugs is effective in the absence of leucocytes.

None of the drugs exhibits any bacteriostatic effect on *Staph. aureus*.

The growth of *N. gonorrhoeae* is retarded by all three drugs in the presence of leucocytes. In de-leucocytised blood soluseptasine still exerts a strong bacteriostatic effect on the organism.

All the drugs are effective against *N. meningitidis* in the presence of corpuscles—in the case of M & B 693 at a dilution of 1 in 60,000. That drug is active at a dilution of 1 in 60,000 even in the absence of blood.

The dependence of these drugs on the presence of leucocytes is in agreement with the findings of Fleming (1938).

From the evidence set forth above it appears that M & B 693 may prove the most useful therapeutic agent in cerebrospinal fever and in conditions arising from infection with *Str. viridans*. Soluseptasine seems the most satisfactory for dealing with *N. gonorrhoeae*.

The drugs used in the above experiments were supplied by Burroughs Wellcome (sulphonamide-P), Dr. Ewins of May and Baker (M & B 693), and Dr. F. G. Hobson, Radcliffe Infirmary (soluseptasine). We wish to express our thanks for these gifts.

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C. D. De Langen, J. C. Boswijk, and C. L. C. van Nieuwenhuizen (*Nederl. Tijdschr. Geneesk.*, **82**, 4970) record an outbreak of ten cases of pellagra in female patients in a mental hospital. Six had refused food, three had already suffered from gastro-intestinal disturbances, and one was under treatment by cardiazol. Nine of the patients were treated with nicotinic acid in doses not exceeding 200 mg. daily; all recovered without any severe toxic symptoms. One patient who was not so treated died.