that the patients presenting themselves there no longer constituted a fair sample of the cases of carcinoma of the cervix in the community at large. We therefore gave up the futile task, and in all our subsequent communications continued to reckon our operability rate at 63 per cent.

There is, however, one group of cases wherein I can with perfect accuracy give the proportion on which I operated—namely, those whom I saw for the first time in my consulting room in private practice.

Between 1910 and May, 1927, I saw at my house 133 women suffering from carcinoma of the cervix, and of this number I operated on 109, or 82 per cent. The results obtained are as follows:

Patients Seen Privately				
Died of operation	...	...	...	10
Lost sight of before 5 years	...	...	...	2
Died other disease before 5 years	...	...	...	1
Died recurrence before 5 years	...	...	...	51
Well 5 years after operation	...	...	...	45
				109

The operative death rate of this group of cases is 9.1 per cent., the relative cure rate (without deductions) 41.2 per cent., and the absolute cure rate 33.8 per cent. It may be argued that this group represents a number of specially picked cases in whom the average advancement of the disease was less than ordinary. The gland involvement rate does not support this suggestion, for of the 109 cases the regional glands were malignant in 41, or 40 per cent., which is only fractionally below the general average. The lower operative mortality is due to the fact that these women, owing to their better social and financial position, were in a less deteriorated state of health than the average patient.

DEATH RATE OF THE OPERATION

The operative mortality of Wertheim's operation in the past was, and often still is, held up as a reproach against it, although for many years now my death rate has been no greater or less than that of certain other operative procedures the performance of which excites no criticism. I have succeeded in diminishing it to a figure which is considerably below that of prostatectomy. Between 1907 and the end of last year I had performed the operation 428 times, and the following table shows how the operative death rate has fallen:

First	100 operations,	20 operative deaths:	20 per cent.
Second	100	13	13
Third	100	16	16
Last	128	12	9

CONCLUSION

According to approved custom I have carried my percentages into decimals, but such meticulousness has little real value, for the figures dealt with are far too small to be beyond the vagaries of chance. A run of good luck puts them up a cipher or two, a run of bad luck puts them down. We can better express the utility of the operation by saying that by its means we can cure (meaning by that term survival for five years) two out of every five patients operated on and one out of every four patients seen.

If we go further and desire to use the term "cure" in its complete sense, we must frame our statement on the ten-year basis, and say that the operation cures one out of every five patients seen and one out of every three patients operated on.

This general statement applies not merely to my own figures, but also to the results published by those other surgeons who have performed the operation on a large

scale and kept count of their patients' after-histories. Moreover, it is a fixed result incapable of material improvement unless the average period elapsing between the incidence of the disease and the time when the patient presents herself can be shortened—which seems to me very unlikely. It might be thought that the marked reduction in operative mortality would be reflected in the end-results, but it is to be remembered that the bulk of the patients dying as the result of the operation are in an advanced stage of the disease, so that of those who now escape operative death only a small proportion escape death by recurrence. Finally, I would emphasize that the cures effected by the operation are obtained from only a proportion of the cases seen by the surgeon. Besides those he selects for operation, a considerable surplus remains out of every hundred seen by him. These inoperable cases are treated by radiation. As a group they are in an advanced stage of the disease, but, nevertheless, a certain small proportion can be salvaged by these means, and this number must be added to the number of operative cures when estimating the total achievement.

REFERENCES

- ¹ *Lancet*, February 8th, 1930, p. 277.
- ² *Australian and New Zealand Journ. of Surgery*, June, 1931.

B. DIPHTHERIAE, GRAVIS AND MITIS

BY

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Anderson, Happold, McLeod, and Thomson, in 1931, described two forms of diphtheria bacilli, *gravis* and *mitis*, the former being associated with the severest cases of diphtheria with a characteristic clinical picture and a high death rate, the latter with milder attacks and a lower death rate. The main bacteriological characteristics of *gravis*, *mitis*, and *intermediate* forms were as follows:

Gravis ferments starch and glycogen; pellicle and granular deposit in broth; grey or grey-black colony on chocolate tellurite medium.

Mitis does not ferment starch or glycogen; uniform turbidity in broth; black colony (often partial inhibition of growth) on chocolate tellurite.

Intermediate does not ferment starch or glycogen; granular growth in broth.

Twelve strains which Professor McLeod kindly sent us behaved culturally in our hands exactly as he described; nine were typical *gravis* and three typical *mitis*.

IMMUNOLOGICAL EXPERIMENTS

Our first interest was in the immunological implications, for the suggestion arose from this work that the ordinary therapeutic antitoxin was relatively ineffective against infection with the *gravis* bacillus. In order to investigate this point we carried out animal experiments with "typical" *gravis* and *mitis* strains, which were either sent to us by Professor McLeod or isolated by ourselves.

Response to Antitoxin

Gravis and *mitis* strains were injected subcutaneously into groups of guinea-pigs, each guinea-pig receiving 60,000 million bacilli. After various intervals, twenty

units of ordinary therapeutic antitoxin (made from Park-Williams 8 bacillus) were injected intracardially (Table I): 112 animals were used.

TABLE I.—Effect of Ordinary Therapeutic Antitoxin (Intracardiac) on Guinea-pigs Previously Infected (Subcutaneously) with *Gravis* and *Mitis* Strains.

Type	Hours Elapsing before Antitoxin given			
	2	4	6	8
Gravis {	$\frac{0}{8}$	$\frac{4}{20}$	$\frac{9}{14}$	$\frac{17}{17}$
Mitis {	$\frac{0}{5}$	$\frac{5}{20}$	$\frac{6}{14}$	$\frac{14}{14}$

Numerator = Number of guinea-pigs died.
Denominator = Number of guinea-pigs injected.

Thirty-four animals which had been infected with *gravis* strains received antitoxin four to six hours afterwards; thirteen died. In the corresponding *mitis* group eleven died. Park 8 antitoxin is apparently as effective in the treatment of *gravis* as of *mitis* infection in the guinea-pig.

Schick-negative Animals and *Gravis* Infection

If Park-Williams 8 antitoxin were ineffective against infection with *gravis*, as suggested, human beings immunized with the usual prophylactics made from the Park-Williams 8 bacillus would have in their blood only Park-Williams 8 antitoxin. Schick-negative individuals might therefore be unprotected against attack by *gravis* cultures. On this supposition the rare cases of "mild or modified diphtheria" in Schick-negative subjects would be predominantly or solely *gravis*.

We took sixty-one guinea-pigs which had been immunized by Mr. Glenny with T.A.M., T.A.F., or formol-toxoid, all prepared with the Park-Williams 8 strain. All the guinea-pigs were Schick-negative, some being only slightly above the Schick-negative level. Into these sixty-one animals thirty-four strains of *gravis* bacillus (dosage—60,000 million organisms subcutaneously) were injected, six of the strains being from McLeod's own collection; fifty-nine of the guinea-pigs lived, and two died. (Presumably the two which died were just above the Schick-negative line and possessed a low immunity, insufficient to protect against the assault of many millions of bacilli injected subcutaneously.) The strains which killed these two guinea-pigs were thereupon each injected into six further Schick-negative cavies: all twelve animals lived. It was therefore reasonable to conclude that animals fully immunized with Park-Williams 8 prophylactics were immune against attack by *gravis*.

Virulence of *Gravis* and *Mitis* Forms

Quantitative subcutaneous tests in guinea-pigs have shown that the *gravis* type is not more virulent than the *mitis* (Table II).

TABLE II

Type	Number of Bacilli Injected in Millions				
	3,000	2,000	1,000	500	250
Gravis... .. {	$\frac{6}{6}$	$\frac{11}{14}$	$\frac{7}{12}$	$\frac{4}{12}$	$\frac{1}{9}$
Mitis {	$\frac{4}{4}$	$\frac{19}{21}$	$\frac{16}{20}$	$\frac{11}{20}$	$\frac{1}{9}$

Numerator = Number of guinea-pigs died.
Denominator = Number of guinea-pigs injected.

Since McLeod had also used rabbits for his experiments we injected groups of rabbits subcutaneously and intravenously with various doses of *gravis* and *mitis* organisms. Sixty-four animals were used, and the mortality in the

gravis group (thirty-two injected: nineteen died) was definitely lower than in the *mitis* (thirty-two injected: twenty-six died).

The above experiments in guinea-pigs and rabbits show that the virulence of *gravis* is certainly not greater than that of *mitis*. Quantitative intracutaneous tests in thirty-two guinea-pigs also failed to show any significant difference in virulence between *gravis* and *mitis* strains. If anything, the more severe lesions were caused by *mitis* strains.

Potency of *Gravis* and *Mitis* Toxins

Does the *gravis* type produce more potent toxin in laboratory media than the *mitis*? We are indebted to our colleague Mr. C. G. Pope for testing this point. Using several media, including one which had recently given the unprecedentedly high value of 60 Lf. for diphtheria toxin, he examined nine *gravis* and six *mitis* strains. With the latter he made toxins from 16 to 20 Lf. in value: the *gravis* strains mostly yielded toxins of 2 to 4 Lf. (with one strain, toxin of 6 Lf. value was obtained). Apparently some *mitis* strains are much more potent producers of toxin in laboratory media than *gravis*.

Severity of Infection and Type

Is *gravis* associated conspicuously with severe and *mitis* with mild infections? Obviously a satisfactory answer will call for the collection of large numbers of figures over a long period. We are indebted to various clinicians in fifteen areas in the British Isles and four cities abroad for sending us cultures. In the following list the first figure indicates the number of swabs, and the second the percentage showing *gravis* type: Cork, 14-90; Ipswich, 10-90; Frankfort, 6-80; Hull, 106-60; various English towns, 48-60; Budapest, 10-40; Bristol, 20-30; Prague, 11-30; London, 53-20; Scotland, 37-15; Copenhagen, 20-0. (We accepted the ability to ferment starch and the formation of pellicle with granular deposit in broth as the criteria of *gravis* strains, even where the other characteristics were not completely typical.) Statistically these figures are of slight value, for from some areas we received cultures only from severe cases, whereas from other areas we received cultures from every case of frank diphtheria. The figures at most indicate that the *gravis* type occurs in many areas.

Of 235 strains so far examined, for which the clinical data were available, 76 were *gravis*, 116 *mitis*, and 43 intermediate. The 192 cases from which *gravis* or *mitis* organisms were isolated were grouped in accordance with the severity of the infection: twenty-one mild cases, 52 per cent. *gravis*; thirty-three moderate cases, 27 per cent. *gravis*; eighty-seven severe cases, 40 per cent. *gravis*; fifty-one very severe cases, 55 per cent. *gravis*. Very severe cases were therefore not associated with a significantly higher percentage of *gravis* strains than were mild cases.

In 167 cases we obtained data as to the patient's recovery or death. Seventy-nine cultures were classified as *gravis* with twenty-eight deaths (a mortality of 35 per cent.); eighty-eight cultures were classified as *mitis* with twenty-seven deaths (a mortality of 30 per cent.). The death rate in both groups, while not significantly different, is high, since at this stage of the investigation we had asked for cultures only from severe or fatal cases. The point of outstanding interest is that, while Anderson and his colleagues had no deaths in ninety-one *mitis* infections in the Leeds area, our results show that some *mitis* infections from other areas were fatal.

DIFFICULTIES IN CLASSIFICATION

It should be mentioned that we found an arbitrary classification of our cultures in some instances difficult. In our whole inquiry we received 347 strains. Of these, 152 fermented starch and glycogen (*gravis*), but in broth only 124 gave

the typical *gravis* pellicle and granular deposit, while 28 showed uniform turbidity, and therefore resembled *mitis*. In 195 strains there was failure to ferment starch and glycogen (*mitis*), but in broth only 118 gave the typical *mitis* appearance, 14 showed pellicle and deposit, while 63 gave a deposit but no pellicle. We also observed colony differences on McLeod's chocolate tellurite medium which do not conform to the Leeds classification.

Our feeling is, therefore, that one can by refinement of methods and readings make a number of groups shading from the typical *gravis* at one end to the typical *mitis* at the other, but so far as we can judge from our limited experience the majority of strains are nearer the two ends of the scale, and can be classified as *gravis* or *mitis*.

DISCUSSION AND SUMMARY

The interesting distribution of *gravis*, *mitis*, and *intermediate* types, and their association with the varying severity of attacks of diphtheria, call for the examination of large numbers of serial cases in different areas.

From the work of Anderson and his co-workers in Leeds the following suggestions have arisen: (a) that the *gravis* type is mainly, or even solely, associated with severe forms of diphtheria; (b) that the *mitis* type causes only mild attacks; (c) that attacks caused by *gravis* strains respond less satisfactorily to the ordinary therapeutic serum prepared from the Park-Williams 8 bacillus, and that a special antitoxin is called for. Suggestions (a) and (b) appear to be true for the Leeds area, but on our data are not applicable to the country generally.

Our results, which are at variance with the suggestions arising out of the Leeds work, may be summarized as follows:

1. If *gravis* and *mitis* cultures are injected into groups of guinea-pigs the two groups can be saved with equal readiness by Park 8 antitoxin given some hours later.

2. Guinea-pigs immunized with prophylactic mixtures which are in current use for human immunization in England and which are prepared from the Park 8 strain survive the injection of large doses of *gravis* cultures.

3. *Mitis* strains are at least as virulent to guinea-pigs and rabbits as *gravis*. Subcutaneous, intracutaneous, and intravenous methods were employed.

4. *Mitis* strains have produced much better toxins than *gravis* under the conditions in which diphtheria toxin is usually produced in laboratories.

5. There is no satisfactory evidence that the gravest types of diphtheria are generally associated solely or even mainly with the *gravis* type of bacillus.

6. It is possible, by the use of the methods described by Anderson and his colleagues, to select a number of groups of bacilli intermediate in character between typical *gravis* and *mitis*.

The interesting association of the *gravis* bacillus with severe attacks of diphtheria found in the Leeds area is a local phenomenon. Since the implications of the term "*gravis*" do not seem to have been substantiated by further inquiry, we would suggest that the name *gravis* be withdrawn in favour of some non-committal title such as "starch-fermenting type."

BIBLIOGRAPHY

- Anderson, J. S., Happold, F. C., McLeod, J. W., and Thomson, J. G.: *Journ. Path. and Bact.*, 1931, xxxiv, 667.
Anderson, J. S.: *Public Health*, 1932, xlv, 198.

BACTERIA ON FRUIT

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One of the most often iterated of slogans, in these days of slogans, is "Eat more fruit." We are exhorted to eat fruit for many reasons—for their vitamin content, for their valuable mineral constituents, and because the indigestible part (usually referred to as ballast) acts as a gentle stimulant to the intestinal tract. Some fruits, again, such as bananas, dates, figs, and so on, which are known as food fruits, are recommended for their nutritive properties. So far as I have seen, however, the public attention in this country is never drawn to the fact that raw fruit is rife with micro-organisms. While I am of the opinion that this omission is reprehensible, it is perhaps too much to expect the advocates of a fruit diet to say anything that might seem to detract from their advice.

In a recent authoritative publication¹ there occurs the statement, "Bacteria, moulds, and yeasts are common on the surface of fruit." No hint is given as to the nature of these bacteria, and one becomes curious as to what they are. Hoder² has carried out a series of examinations on different fruits obtained in the market and from street traders in Prague. The object of his investigations was to estimate the bacterial content of fruit and to show the great diminution that takes place after washing the fruit. The fruit was washed three times in normal saline and plates inoculated from each washing. The result was an enormous count from the first washing, a marked diminution from the second, and a further decrease from the third. To give an example, from three cherries after the first washing the count was 26,000, after the second 700, and after the third 3. He proceeded to carry out a similar experiment, using water instead of saline. Again there was a spectacular decrease in the bacterial count between the first and second washings. As to the organisms present, he mentions the occurrence of *B. proteus*, *B. coli*, *B. subtilis*, staphylococci, strepto-

cocci, sarcinae, yeasts, moulds, and Gram-positive and Gram-negative bacilli. In conclusion, he recommends that raw fruit should be washed in ordinary drinking water at least once. Sartory-Filassier (1909) also found that the bacterial count was markedly decreased by repeated washing. In my own investigations three kinds of fruit were used—namely, dates, grapes, and cherries. As the aim was not to estimate the bacterial content, but to find out the nature of the organisms present, the following procedure was adopted.

By means of sterile forceps the fruit was introduced into flasks of ordinary broth, which were then placed in an incubator at 37° C. The following day a loopful of the broth was inoculated on a MacConkey plate. A blood-agar plate was similarly treated. A tube of sterilized milk and a maltose agar slope were also inoculated.

Experiment I.—Dates

The dates examined were obtained in boxes or packets, and may conveniently be divided into Tunis dates and Iraq dates. The former were French packed, while the latter were either British packed or packed locally in the country of origin. The Tunis dates, comprising six different brands, were in oblong boxes in two layers, the top layer being covered with a strip of transparent paper as if to give an impression of cleanliness. The top layer was discarded, and ten or twelve dates were taken from the bottom layer and put into two flasks of broth. The cultural findings were as follows:

Tunis Dates (16 Examinations)

Nature of Organisms	Times Isolated
<i>B. subtilis</i> and allied organisms ...	16
Streptococci ...	16
Yeasts ...	8
<i>B. coli</i> ...	7
Staphylococci ...	7

The biochemical reactions of the streptococci were tested, and by the Holman classification, which is sufficient for our present purpose, were found to be *S. faecalis* (12), *S. mitis* (9), *S. equinus* (2), *S. salivarius* (2). The figures in brackets denote the number of samples from which obtained.

The heat-resistance test was carried out (half an hour at 60° C.). *S. faecalis* was heat-resistant. In my experience *S. mitis* was sometimes resistant and sometimes not.