it will probably spring from outside our own science, and from the sphere of physics or chemistry, and we may have difficulty at first in apprehending it. We need, therefore, at the present day, not only observers and experimentalists, but bridge-makers who will mediate between the laboratory and the bedside, and who will interpret and apply the work of the pure physiologist, physicist, or chemist, in so far as it bears upon practical medicine. Such men have always been few, and they must tend to get fewer as the sciences ancillary to medicine become more and more specialised; but the greater the divorce of medicine from pure science, the more are such bridge-makers necessary. How they are to be found and trained, and what position they are to occupy, are questions for the future, but that men capable of acting as liaison officers in the scientific army are necessary there can be no doubt. Nor can it be doubted that they could contribute materially, if not spectacularly, to the advance of medicine.

But most of all we need thinkers. Observation and experiment can give us facts, have indeed given us too many facts. What we require is men with imagination, men of the contemplative type of Harvey, fertile in hypotheses, who can see the inter-relation between the facts and who can bind them into manageable sheaves and induce from them those generalisations which we call natural laws.

Great generalisers, of course, are men of genius and cannot be produced to order. They flourish in some epochs more than in others, for there are, as Bacon said, waste tracts in time as well as in space. It may be that we are in such a waste tract now. Certainly men of great imaginative genius do not seem to be relatively so abundant as they were in the time of Harvey; perhaps the intellectual climate of to-day does not favour their appearance. I have already spoken of the restlessness and distractions of our day and their unfavourable effect on thought, and one might add to this obstacle the contempt for the humanities and for pure knowledge characteristic of a civilisation directed to merely material ends. It may be doubted, too, whether our present methods of education are favourable to the production of men of the type we most need. To give up early the humane studies and take to specialism is not the way to train the imagination, and tends to result in the production of skilled technicians rather than of educated men. Be this as it may, there is reason to expect that the clinical atmosphere will be more favourable to the production of generalisations than that of the laboratory. For the gifts of judgment and insight, the power to see the wood and not merely the trees, so necessary for fruitful generalisation, are just those required by the diagnostician. The clinical atmosphere, however, must be a wide one, for specialism is not conducive to the large and general view.

I would conclude by urging upon all the toilers in the field of medical science the necessity for unity. We need every worker, whether at the bedside or in the laboratory, who is sincerely seeking the truth as Harvey understood it, for in the house of Science there are many mansions. Let us not say I am of Paul; and I of Apollos, and I of Cephas; let the experimentalist not despise the clinical observer as superficial, nor the clinician the laboratory worker as narrow, nor let both contemn the thinker as visionary and unpractical. Let me rather exhort all, as I am bidden this day in Harvey's name to exhort the Fellows of this College, that they continue in love and affection amongst themselves.

THE SERUM THERAPY OF PLAGUE.

BY B. P. B. NAIDU, M.D. EDIN., M.H., D.P.H., D.T.M. LIVERP.,
AND
F. P. MACKIE, K.H.S., O.B.E., M.D., M.SC., D.P.H. BRIST., F.R.C.S. ENG., F.R.C.P. LOND.,
BREV. COL. I.M.S.

(From the Haffkine Institute, Bombay.)*

ALTHOUGH bubonic plague has been raging in India for nearly 35 years, its treatment has hitherto remained symptomatic. It is true that a considerable measure of success has attended the prevention of the disease by the use of Haffkine's prophylactic, but attempts, whether in India or elsewhere, to produce a curative serum have hitherto been disappointing. That great desideratum, a bactericidal drug which shall effect sterilisation by intravenous medication, has been sought assiduously, but not found. Work on these lines has been carried on in the Haffkine Institute, and a number of substances—particularly of the mercuri-phenol group—have been synthesised by Caius and others of this laboratory, but even when they have been found in vitro to possess very high bactericidal action on *B. pestis* this action has not been found transferable to the living animal.

Haffkine's vaccine, whether plain or sensitised, has likewise been found to be ineffective once the course of the disease has started. The successful results recorded by d'Herelle in Alexandria in 1925, following the use of his anti-pest bacteriophage, raised great hopes, but when this remedy was subjected to a careful trial in India it proved ineffective and did not influence either the course of the disease or the case-mortality. Successful results have been recorded from the use of plague serum outside India, but when this method has been used in Indian hospitals the results have not been so satisfactory (vide Table I.). Whether this is due to the greater virulence of *B. pestis* in India or to some other factor is not clear, but d'Herelle, in his work on plague-phage, found that strains of *B. pestis* isolated in India were much more virulent than those from other sources.

A careful analysis of the results obtained by the use of various preparations of sera in our hospitals during the years 1897–1912 showed that their administration was attended by a reduction in case-mortality of not more than 7 to 10 per cent. The Advisory Committee on Plague Investigations in India reported in 1913 that, as a result of an inquiry into the matter, "the administration of the available sera is not a practical means of bringing about any material diminution in the mortality from plague; it may well be that better results will be obtained if the treatment could be commenced within a few hours of the onset of the disease; this, however, is in the great majority of cases impossible in ordinary hospital practice." The figures relating to these trials are given in Table I.

Choksy (1923), of Bombay, who has had unrivalled experience of the treatment of plague in India, found a moderate reduction of 10 to 20 per cent. in case-mortality from the use of anti-pest serum, and urged further research regarding its manufacture, on the ground that "it is the only remedy that holds out

* This investigation, which has been carried out during 1927–31, has been financed throughout by the I.R.F.A., to whom we are indebted for permission to publish these preliminary results.

any hope of reducing the excessively high case-mortality which has so markedly characterised the epidemics at Bombay."

In 1927 a fresh attempt was made at the Haffkine Institute to approach this problem, and one of us (B. P. B. N.) was put on special duty under the auspices of the Indian Research Fund Association to carry out the investigation. Our previous work on plague vaccines showed us that the first necessity is to use the most virulent strains of *B. pestis* available, and to see that they retain their high degree of virulence throughout the process of vaccine manufacture.

TABLE I.

Compiled from the Reports of Bannerman and the Advisory Committee, Plague Investigations in India. Conditions of trial were reasonably accurate, controls being strictly comparable with the serum-treated.

Various sera tried in plague hospitals.	Years.	Treated.		Controls.	
		Cases.	Case-mort. %	Cases.	Case-mort. %
Yersin's ..	1897–1907	226	74·3	231	70·5
,, ..	1908–1910	146	65·1	146	71·9
Haffkine's ..	1897–1898	100	+14·0*	100	—
Lustig's ..	1897–1903	608	71·7	609	79·1
Terni's.. ..	1901–1904	110	80·9	110	81·8
Brazil's ..	1902–1904	70	82·8	70	85·7
Rowland's ..	1911–1912	76	68·4	76	77·6

* Mortality 14 per cent. higher than in controls.

These requirements we summarised as follows: (1) the immunising value of a vaccine is largely dependent on the virulence of the strain employed for its preparation; (2) strains isolated either from human cases or from experimentally infected rats exhibit individual variations in virulence; (3) emulsions made from plague-infected spleen are more virulent than those obtained from cultures on agar or in broth; (4) virulence of the strain is lost wholly or in part under prolonged cultivation on artificial media; (5) virulence of the organism is modified by passages from a highly susceptible animal into animals of relatively low susceptibility; and (6) an avirulent strain produces a vaccine of low potency.

The next desideratum in the production of serum is the choice of an animal which is naturally susceptible to the pasteurella group of organisms or which is readily susceptible to *B. pestis* by inoculation. Hitherto the horse has been the animal of choice, and the anti-plague sera of Yersin, Roux, Kolle, Lustig, and others were made from this animal. Haffkine (quoted by Bannerman, 1905) found that sheep produced a better serum than horses, whilst Terni (quoted by Bannerman) in Messina produced a more potent serum from mules and cattle than from horses. To what extent the susceptibility of an animal to infection by a particular organism influences the production of a potent serum is a subject which seems to have received little attention, but we decided to discard the horse and to attempt the production of serum from bovines and sheep, on the ground that they are animals naturally liable to pasteurella infection.

For convenience, we first used rabbits, which are highly susceptible to plague and to other pasteurella infection by laboratory methods, and we were able to immunise these animals to a point when they would withstand a dose of one agar slope a week of living virulent plague bacilli by intravenous injection over a period of two years. Incidentally, we found that immunisation by the subcutaneous route produced a lower grade serum than by the intravenous route. Serum from these immunised rabbits was then used as a curative measure in other plague-infected rabbits. The serum was administered in quantities not exceeding 2 c.cm., either as a single dose or in similar amounts at intervals of 24 hours, with the results shown in Table II.

TABLE II.

Time of administration of serum after infection.	Infected rabbits.	Mortality within 30 days after infection, per cent.
Immediately after ..	34	0
24 hours ,, ..	40	0
48 ,, ,, ..	43	9·3
72 ,, ,, ..	48	31·2
96 ,, ,, ..	25	32·0
Controls	33	94·0

From this it will be seen that all the animals were cured when the serum was given up to 24 hours after infection, and even when treatment was delayed until 96 hours after infection, when the animals are severely ill or even moribund, the serum saved two-thirds of the rabbits as compared with the controls. This experiment showed us that it was possible to manufacture an anti-plague serum of high curative value in animals of the same species, and the next thing to attempt was to produce serum from a large animal which would act similarly on those of a different kind.

Sheep were then tried, and were found to be very susceptible to plague. We inoculated 12 sheep with intravenous doses of virulent *B. pestis* varying from 0·003 mg. to 0·018 mg. of spleen substance of a rat which had died of plague. Six of the sheep died, five within 11 days of infection, with signs of acute plague. We now began the immunisation of sheep, using virulent cultures intravenously in graduated doses at weekly intervals, working up from 1/20th of an agar slope to 50 agar slopes at a dose. In the course of this very severe test most of the sheep died, and at the end of 16 months only three remained out of the original 21 animals. This sheep serum was then tested for its curative properties, side by side with the anti-plague serum of the Pasteur Institute at Paris, on a batch of 800 infected Madras rats. The results are seen in Table III.

TABLE III.

Time of administration of serum after infection.	Dose in c.cm.	Sheep serum.		Pasteur Institute serum.		Controls.	
		Rats.	Mort. %	Rats.	Mort. %	Rats.	Mort. %
Immediately after	1	100	13·0	100	52·0	85	88·2
24 hours after ..	1	100	43·0	100	83·0	100	90·0
	2	100	23·0	100	72·0	100	91·0
	3	100	32·0	100	77·0	100	97·0
Total	—	400	27·7	400	71·0	385	91·7

The results show that sheep serum is about two and a half times as potent as the Pasteur Institute serum, and saves the lives of about two-thirds of the infected rats, even when its administration is delayed for 24 hours.

Owing to the heavy mortality amongst sheep and their relatively small yield of serum, we next turned our attention to calves. We began with two eighteen-months-old calves weighing each about 300 lb. and injected them with living virulent plague cultures by the intravenous and subcutaneous routes. The latter gave too severe local and general reactions, so

subsequently the intravenous route was used. As in one calf the dose was too rapidly increased (it died after the seventh injection when 40 agar slopes were given in a single dose), the other calf received more gradual doses, and it survived. It was bled at the end of 12 months when it had received 38 intravenous injections, beginning with one-fifth of an agar slope and ending with 100 slopes at a dose. The therapeutic value of its serum was then tested on 250 rabbits and 40 controls, side by side with the anti-plague serum of the Pasteur Institute of Paris. The results are shown in Table IV.

TABLE IV.

Time of administration of serum after infection.	Calf serum.		Pasteur Institute serum.		Controls.	
	Rabbits	Mort. %	Rabbits	Mort. %	Rabbits	Mort. %
48 hr. after, 1 c.cm. on 3 suc. days..	50	18·0	50	52·0	10	100·0
72 hr. after, 2 c.cm. on 3 suc. days..	50	24·0	50	64·0	10	100·0
72 hr. after, 1 c.cm. once	25	24·0	—	—	10	100·0
72 hr. after, 2 c.cm. once	25	16·0	—	—	10	100·0
Total	150	20·7	100	58·0	40	100·0

suc. =successive.

We regarded these results as very promising, in that our serum saved 80 per cent. of rabbits compared with the controls, and that such a small dose as 2 c.cm. saved over 80 per cent. of rabbits in which the infection had remained unchecked for 72 hours. The Haffkine Institute serum was nearly three times as potent as that prepared by the Pasteur Institute of Paris.

At this stage, acting on a suggestion of Dr. G. F. Petrie, of the Lister Institute, we carried out a comparative test on the value of their serum with the Haffkine Institute and other anti-plague sera. This experiment involved the use of 1768 Madras rats. The results are seen in Table V.

TABLE V.

Sera tested.	Protective value.	Antitoxic value.	Curative value.
	Rats used—		
	560	650	558
Unconcentrated.	Mortality, per cent.		
Lister Institute—			
"Armistice"	100·0	43·0	93·0
"Rowland"	29·0	30·0	39·0
Pasteur Institute.. ..	70·0	52·0	65·0
Haffkine Institute—			
Sheep	0	0	3·3
Calf	10·0	0	5·0
Normal horse	97·0	90·0	93·0
Concentrated—			
German "A"	42·5	—	77·5
German "B"	45·0	—	65·0
"Rowland"	20·0	—	37·5
Reconcentrated—			
"Rowland"	15·0	—	81·6
Controls	97·5	95·0	92·5

These results showed that the Haffkine Institute sera had much greater protective, antitoxic, and curative value than any of the other sera. The reconcentration of the Lister Institute serum "Rowland" appears to lessen its curative property very considerably.

AGGLUTINATION AND PRECIPITATION TESTS.

The normal sera of sheep, calves, and horses do not agglutinate the plague bacillus. The immune serum from sheep agglutinates living plague bacilli in a dilution of 1 in 64, that from calf in a dilution of 1 in 256, while that from the horse obtained from the Pasteur Institute and the Lister Institute fails to agglutinate these bacilli even in a dilution of 1 in 2. Experiments carried out with the filtrate of a six weeks' broth culture of *B. pestis* showed the presence of precipitins in the sera of immunised sheep and calves. These precipitins were absent from the anti-plague sera obtained from the Pasteur Institute and the Lister Institute, and also from normal sera of sheep, calves, and horses. Thus the anti-plague sera of the Pasteur Institute and the Lister Institute contain neither agglutinins nor precipitins for our local strains.

With this preliminary work as our guide, we were ready to undertake the crucial experiment on the attempted cure of human plague. By February, 1931, we had five sheep, three bullocks, and four buffaloes fully immunised. They had received 35 to 45 injections during the preceding 12 months, having reached a final dose of 100 agar slopes at each infection in the case of sheep and 200 slopes for buffaloes and bullocks. Before using the serum for human cases we carried out a short experiment to ensure the stability of the stored serum. Rabbits were given a dose of 1 c.cm. on three consecutive days, 48 hours after the infecting doses of *B. pestis*. The results were:—

Bullock serum ..	11 rabbits ..	mort. %	18·0
Buffalo serum ..	18 „ ..	„	11·1
Controls	8 „ ..	„	100·0

These results satisfied us regarding the retention of potency.

Use of the Serum in Human Plague.

An outbreak of plague at Hyderabad (Deccan) furnished an opportunity to try the effect of our serum on human cases. By the kindness of Colonel Norman Walker, I.M.S., and the staff of the Plague Hospital, we were able to carry out some observations on scientific lines. At first every alternate case admitted to the hospital was given serum and the control case treated with all the other usual therapeutic measures except serum. Later, every third admission was taken as a control for, as the efficacy of the treatment became apparent, much pressure was brought to bear on us to abandon the use of controls, and medical men refused to send cases unless serum treatment was guaranteed. We were able to observe the course of the disease in 76 cases which could be divided into three classes: (*a*) cases with heavy *B. pestis* septicæmia; (*b*) cases with light septicæmia or pure bubonic cases; and (*c*) cases diagnosed clinically as plague but not bacteriologically confirmed.

Of the 76 cases, 43 were treated with serum, with 15 deaths, and 33 controls without serum, of which 23 died. Table VI. shows the disposition of the cases.

Regarding Class A, the septicæmic class, it has always been held that the presence of any considerable number of *B. pestis* in the circulating blood was the invariable presage of death. A reference to Table VII. will reveal that all previous experience in India shows that such cases gave 100 per cent. mortality, and our 17 control cases all died, whereas four out of 15 recovered under serum treatment. Apart from recovery, some striking bacteriological

observations were made on cases which ultimately succumbed, in that the septicæmia was observed to lessen or to disappear entirely under serum treatment, whereas in cases which received no serum septicæmia, once established, increased up till the

TABLE VI.

Class.	Cultural diagnosis.		Under serum treatment.		Controls (without serum).	
	Bubo.	Blood.	Cases.	Deaths.	Cases.	Deaths.
A	+	+ + +	10	7	8	8
	−	+ + +	1	1	3	3
	+	+ +	3	2	4	4
	−	+ +	1	1	2	2
Total			15	11 (73·3 %)	17	17 (100·0 %)
B	+	+	7	1	3	2
	−	+	1	0	1	1
	+	−	11	3	4	1
Total			19	4 (21·0 %)	8	4 (50·0 %)
C	Clinically plague, not bacteriologically confirmed.		9	0	8	2 (25·0 %)

+ =less than 10 colonies in 0·25 c.cm. of blood.
+ + =less than 100 ,, ,, ,,
+ + + =100 colonies and over ,, ,,

time of death. Death in the former group of cases was attributable to myocarditis or other toxic manifestations resulting from the previous septicæmia.

Class B, which includes the cases of moderate severity, also yielded interesting information, though the numbers are very small. It is in this class that we should expect to save the largest percentage by serum treatment. It includes the early or slight septicæmic cases (those with less than ten *B. pestis* in a quarter of a c.cm. of blood) and the bubonic cases without generalised infection at the time of examination. The factor responsible for death or recovery in plague is probably septicæmia and, if the infection remains localised either naturally or as a result of serum therapy, the recovery of the patient may be expected. We believe that the prompt administration of serum will prevent this blood infection and, as we have shown, may sterilise the blood even when early septicæmia has occurred. Thus in the small group of eight cases with early septicæmia, seven recovered under serum treatment, whereas only one out of four recovered without serum. The relationship of septicæmia to recovery under serum therapy is set out in Table VII.

TABLE VII.

Septicæmic cases in hospital admissions.		Berestneff and Mayr, Bombay, 1901. Lustig's serum.				Plague Commission, Bombay, 1908–12. Sera of Pasteur Inst. and of Lister Inst.			
Class.	Cultural diagnosis of blood.	Tr.	Mort. %	Cl.	Mort. %	Tr.	Mort. %	Cl.	Mort. %
A	+ + +	6	100·0	9	100·0	75	100·0	81	100·0
	+ +	9	100·0	5	100·0	15	100·0	24	100·0
B	+	28	78·6	9	77·7	47	74·5	47	74·5
B+C	0	28	71·4	10	50·0	85	25·9	70	34·3

See note under Table VI. Tr. =treated; Cl. =control.

These results show that in former experiments carried out in India three out of every four cases died with the mildest or earliest degree of blood infection, whilst of those which have had more than 40 *B. pestis* per c.cm. of blood every case has died.

Class C included 17 cases of undoubted plague from which *B. pestis* was not recovered; all nine cases treated with serum survived, whilst two out of eight control cases died.

We began by giving doses of 100 c.cm. of serum, but we very soon found that this large amount of protein, when injected intravenously in one dose, was sufficient to embarrass if not to endanger the heart already poisoned by plague toxins. The fact that two cases in Class B died within two hours of injection suggests that these large doses may have precipitated the fatal result. Subsequently the dose was reduced to 60 c.cm. on admission, with a further dose of 40 c.cm. on the next day. In three cases repeated doses had to be given for several days, and it appears that if this practice could always be carried out more cases might be saved. From the clinical point of view the improvement of some cases under serum treatment was remarkable, the fever going down, eyes becoming clear, delirium disappearing, and the heart improving in tone within a few hours of the administration of the serum.

Remarks.

In this paper we have endeavoured to give a brief account of the laboratory work which led up to the use of this anti-plague serum on human cases and, whilst the former shows conclusively that a potent serum has been produced, the human experiment, though very favourable, is inconclusive, in that the numbers were too small to carry statistical weight. The fact that the plague season in India has ended for the time being, and the removal of one of us (F. P. M.) to another sphere of duty, decided us to publish these results in the form of a preliminary report.

It may be argued that, as the epidemic was on the decline, our results were thereby vitiated, but the force of that argument is lessened in that we compared our cases with controls admitted alternately to the plague wards, and the careful observations on septicæmia in themselves provided a still more accurate standard of comparison. The paucity of cases was unavoidable, and though we made every effort to extend the range of observation during the plague season just past we were unable to find any area where a sufficient number of cases could be got together under conditions suitable for a more conclusive scientific experiment.

Conclusions.

1. It has been found possible to produce a more potent anti-plague serum than any that has hitherto been available. In preparing this, attention was paid to three points which are considered to be of importance—namely, the choice of the animal, the virulence of the strain used, and the method of immunisation.

2. Cattle were chosen rather than horses, on the ground that they are naturally susceptible to organisms of the pasteurella group.

3. A highly virulent strain of *B. pestis* was used in the production of serum.

4. The serum of immunised cattle was found to possess good agglutinative power and to be possessed of antitoxic as well as antibacterial properties.

5. The use of this serum as a curative measure resulted in the saving of the lives of a high proportion of rats and rabbits as compared with the controls.

6. In all these desirable properties the Haffkine Institute serum was shown to be far superior to any other anti-plague serum tested.

7. When applied to a small human epidemic the results were very promising. Out of a total of 76 cases, 43 were treated with serum, generally in one dose, and of these 15 died, whilst of the controls (alternate cases) 23 out of 33 died. Several cases with advanced *B. pestis* septicæmia recovered, and 7 out of 8 cases with early septicæmia survived, as compared with an invariable fatality in the former group and 75 per cent. mortality in the latter. We anticipate that the use of the Haffkine Institute serum will save the majority of lives in Classes B and C, and favourable conditions for a large-scale trial on these lines are awaited.

THE ASPHYXIAL ELEMENT IN GAS-OXYGEN ANÆSTHESIA.*

By A. H. Macklin, O.B.E., *M.C.*, M.D. Manch.,
ASSISTANT PHYSICIAN, LATE ANÆSTHETIST, DUNDEE ROYAL INFIRMARY.

In a previous paper [1] I have given the result of a series of 200 cases anæsthetised by nitrous oxide and oxygen. The present paper brings the number to 553, which may be classified as follows:—

Upper abdominal (61).—Gall-bladder, 23; gastro-enterotomy, 13; perforated gastric and duodenal ulcer, 16; pyloroplasty, 2; partial gastrectomy, 1; high laparotomies, 6.

Lower abdominal (175).—Appendicectomy, 136; acute obstruction, 1; ovariotomies, 3; hysterectomies, 2; hysterotomies, 2; laparotomies (various), 31.

Non-abdominal (317).—Hernia and hydrocele, 42; bone plating and wiring, 20; anal and rectal, 21; suprapubic, 7; cystoscopies, 5; amputations (various), 6; nephrectomies (lumbar), 15; empyema, 5; radical amputation (breast), 7; neck operations, glands, &c., 13; mouth operations, 9; dental, 41; thyroidectomies, 3; ophthalmic operations, intra-ocular, 2; extra-ocular, 2; mastoid, 1; various, 118.

With the exception of a few of the earliest cases in the series, and a number of intratracheal cases shortly to be referred to, no agents other than nitrous oxide, oxygen and carbon, dioxide were used. The figures show that a very wide range of cases has been dealt with, including not only a variety of operations, but all sorts and conditions of patients, taken without any attempt at selection, just as they arrived in the anæsthetic room. Particularly I would call attention to the abdominal, the dental, and the ophthalmic cases. Of the last-named, two were for buphthalmos, a condition of increased ocular tension involving an operation of great delicacy. Though the total number is small, I think the series must be regarded as a very severe test of any anæsthetic agent.

I have no reason to modify my earlier opinion of the overwhelming advantages of gas-oxygen in the first and third stages—i.e., the induction and post-operative periods—as compared with ether and chloroform; the evidence of patients, and also of ward sisters and nurses, makes this so clear as scarcely to need discussion. During the operative stage, however, it has not been possible to demonstrate such marked superiority; the most rapid enthusiast could never make such a claim. Nevertheless, in spite of assertions appearing from time to time in medical journals and in text-books to the effect that gas-oxygen cannot be relied upon to give adequate anæsthesia in robust adults, my series has shown quite conclusively that it is possible with this agent to produce relaxation sufficient to allow of even high abdominal operations being carried out on any kind of patient.

Upper abdominal operations provide the crucial test of any anæsthetic agent; in no other group of cases is such complete relaxation required. Of this group of cases in my series I would say that in one-third relaxation was good, and, as we say, "the patient took the anæsthetic well." In another third the relaxation was satisfactory, but the patient did not perhaps "take the anæsthetic so well," and the anæsthetist rather "sweated" (I know of no more descriptive term) over the effort to keep things going. In the final third the course of the anæsthetic was jerky, the anæsthetist did not succeed in completely eliminating those catchings of the breath and spasmodic contractions of the recti muscles which occur, for example, when the stomach is pulled forward or the gall-bladder pressed upon—little troubles with which some of us are only too familiar—and before edges of peritoneum could be brought together in the lax, easy way that the surgeon desires it was necessary to resort to secondary saturation, which, though remarkably effective, requires momentarily a very deep, and probably dangerous, asphyxiation. These cases I cannot look back upon as being by any means satisfactory. I kept notes of them, and I think that one-third good, one-third reasonable, and one-third bad represents fairly the results in upper abdominal surgery during the operative period. Even with the worst of them recovery was extraordinarily rapid, and, personally, I never failed to feel a glow of satisfaction at the condition of these patients in the post-operative period as compared with those that had been etherised or treated with other toxic agents.

COMPARISON WITH OTHER ANÆSTHETICS IN UPPER ABDOMINAL SURGERY.

Ether, I think, is generally recognised as the agent capable of producing the most complete relaxation, and may be usefully selected for comparison. For several years I used ether as a routine agent, by open, closed, and semi-closed methods, with and without local anæsthesia, and though I did not then take such careful notes as I have since done with gas-oxygen, I would estimate that in not less than one-third the relaxation, if one may judge by the crucial test of peritoneal suture, was not satisfactory to the surgeon or a source of complacency to myself. Of course, the personal factor cannot be eliminated, and it is likely that other anæsthetists would claim better results, but during visits to theatres in different parts of the country I have seen others struggle with the difficulties which I have so often encountered.

My series of upper abdominal cases includes 16 in which gas-oxygen was given by the endotracheal route, and these approached more nearly to the ideal than any others I have given. This method, in my opinion, is the one which is most likely to satisfy the immediate needs of the surgeon, just as, incidentally, as soon as the trachea is entered, it eliminates nearly all the troubles of the anæsthetist. The technique is undoubtedly difficult, since probably few anæsthetists possess the dexterity necessary to effect the passage of a catheter through the vocal cords without having recourse to an anæsthetic less evanescent than gas. In more than half of my own cases I found it necessary to use chloroform (which I preferred to ether) during induction, to get a sufficiently lasting relaxation of the throat muscles. These cases thus form an exception to the rest of the series, in which no anæsthetic other than nitrous-oxide was used. Heavy preliminary "doping" is neither necessary

* Read before the Forfarshire Medical Association.