HOMOLOGOUS ANTIPNEUMOCOCCAL SERUMS IN THE TREATMENT OF LOBAR PNEUMONIA

BY

RICHARD R. ARMSTRONG, M.D., F.R.C.P.

AND

R. SLEIGH JOHNSON, M.D., M.R.C.P.

Serum treatment of lobar pneumonia is no new thing. Fresh interest has been aroused in this subject during recent years by the use, in America, of the "Felton" concentrated antipneumococcal serum. Reports have appeared very recently, from Edinburgh and Glasgow, of the therapeutic application of the concentrate in cases of lobar pneumonia due to infection by the pneumococcal Types I and II. It has been our good fortune, thanks largely to the Medical Research Council, to try this new remedy during the past few months. It will be evident from the account which follows that we believe the antipneumococcal serum to be a remedy of the first importance. There is, however, a strong body of opinion, concerned not so much with clinical evidence as with crude mortality statistics, which inclines to doubt this conclusion, particularly in view of the fact that the mortality, in cases due to Type II infection, has not been shown to be materially reduced. On our part, we seriously doubt whether crude mortality experience affords a true criterion by which the success of this treatment may be judged, for every physician will agree that a great variety of conditions may prejudice the course of pneumonia and lead to the death of the patient, irrespective of the pulmonary condition.

THE FIELD OF INQUIRY

The field of inquiry was limited at first to St. Bartholomew's Hospital. It soon became apparent that the number of cases likely to be available there was small. Grateful thanks are due to the Medical Officer of the London County Council for permission to work, since mid-January, in the Council's highly efficient and well-equipped hospitals at Mile End and Bermondsey; acknowledgements are due to the medical superintendents at each of these hospitals for unrestricted access to cases, and to the members of their medical and nursing staffs for loyal co-operation. Foremost among our allies has been Dr. Gordon Sears at Mile End, whose balanced judgement of the clinical aspect of treated cases has been of superlative value to us. Some cases at the Victoria Park Chest Hospital were also treated.

RAPID METHOD OF DETERMINING PNEUMOCOCCAL TYPE

So far as we know at the time of writing, the basis of our inquiry differs from that adopted in any other investigation of the kind in this country, in that we have determined before administration of serum the serological type of pneumococcus responsible in each case. The method has already been described in a recent number of the *Journal* (February 7th, p. 214). In brief, a mouse is inoculated with the patient's sputum; in four hours or less the animal's peritoneal cavity is explored by acupuncture. The exudate so obtained is mixed on a slide with an equal volume of each of the type agglutinating serums and examined under the microscope. A characteristic change in the appearance of the pneumococci takes place in the case of a positive reaction. The cocci become conspicuously enlarged; if present in considerable numbers they speedily agglutinate. The reaction is quite characteristic and free from ambiguity. Thus in no instance was serum administered unnecessarily, as happened in other hands, in cases due to infection by nondescript pneumococci.

METHOD OF ADMINISTRATION: SENSITIZATION

The most important consideration in serum treatment must be early administration of the largest convenient dose. In the first instance, intravenous medication is essential; by no other route may the desired result be attained. The suggestion of intravenous serum therapy conjures up the dread of anaphylactic shock. This dread is imaginary rather than real; it ceases to be of importance if the simple procedure be observed of keeping a hypodermic syringe containing 1 c.cm. of 1 in 1,000 adrenaline solution always in readiness before giving the serum. One of our patients had a very severe anaphylactic reaction, but this was promptly controlled by subcutaneous adrenaline. It is the rule that first reactions are the most severe, and that subsequent inoculations progressively provoke less shock; the same generalization applies to the rigors and other forms of disturbance of less moment which are occasionally seen. The elaborate tests for sensitization by dropping serum on to the eye or by squirting it into the skin are, we venture to state, as unnecessary as they are apt to be misleading.

VARIOUS SERUMS USED

The serums used have come, partly by gift and partly by purchase, from different sources; our supplies have been very strictly limited. Our gratitude for the gifts is not the less sincere from the fact that we are not at liberty to divulge the donors' names. A concentrate containing antibodies against the pneumococcal Types I and II prepared by Parke, Davis and Co. or by Lederle was used. A similar concentrate, effective only against Type I pneumococcus, from the Wellcome Laboratory, was also given. These concentrates are alike prepared by the Felton method, being derived from the serum protein of immunized horses by precipitation of the euglobulin fraction, associated with the specific antipneumococcal antibodies, in a large volume of distilled water, the precipitate being collected and redissolved. The protective values, per maker's dose (the contents of each phial supplied), of the three concentrated serums used have been accepted for the purpose of this inquiry as approximately equal, a practice which has been justified by the clinical results.

An unconcentrated (horse) serum, Type I, supplied from the Wellcome Laboratory, was also used by us in four cases. This serum was of exceptionally high titre, and was said to be of nearly two-thirds the protective value of an equal volume of the same firm's concentrate. The preparation of concentrate is both difficult and costly, so that therapeutic trial of this unconcentrated serum was not without point. Seeing that the primary object of treatment is administration of the largest possible quantity of antidote at the earliest moment, the conditions of the experiment are scarcely satisfied by the use of the unconcentrated remedy. This view was confirmed by experience in two cases, although in two others of less severity the results were all that could be desired. We concluded that unconcentrated serum should be used only in early cases of moderate severity or in adolescents whose illness it might be desired to abort.

DOSAGE

The considerations which have determined the size and spacing of doses must now be discussed. The reports from Scotland state that a wide range of doses from a minimum of one dose to a maximum of twenty-six was employed there, with an average of six doses per case. Our impression of the system adopted in America is that there five doses per case represented the average requirement.

Although in many cases improvement follows intravenous injection of the remedy, without any disturbance

of the patient's general state, rigors are of frequent occurrence, particularly in cases treated early in the disease. The severity of the reaction seems proportional to the dose. We find that the contents of two phials (a double dose), approximately 20 c.cm. volume, administered with an ordinary 20 c.cm. glass or Record syringe, is generally the maximum desirable; this dose should be given slowly and cautiously at first. With a sensitive patient or in one subject to bronchitis or asthma, it is better, in our experience, to reduce the dose to one phial. The same conditions apply to the spacing of doses, for if the reaction be severe, six hours is all too short an interval; eight hours is preferable, and in early cases we have been quite content to begin with a double dose morning and evening, a manoeuvre very convenient to the practitioner, who is likely in any event to see his patient twice a day during the acute stage of the pneumonia. Our standard procedure has therefore become: in early cases, an initial double dose followed by a second similar dose, then a final single dose; administration at eight- to twelve-hour intervals; in later cases, three double doses and a final single dose. These doses have generally sufficed, but it must not be supposed that we have been constrained by any arbitrary considerations, as in every case the clinical indications have been our guide. Thus, in some, three doses have aborted the illness; while in one case of exceptional severity nine were given. In general terms, however, if a favourable effect does not follow a course of seven doses, we seriously question whether benefit is likely to follow prolongation of serum treatment.

ANALYSIS OF CASES

Clinically typical cases of pneumococcal primary lobar pneumonia in adult men and women have been exclusively selected for study or treatment. The series includes no children or old people. The incidence of the pneumococcal types of infection is shown in the table.

Incidence of Pneumococcal Types

Type I		Type II		Type III	Nondescript	Total Cases Investigated
Treated	Untreated	Treated	Untreated			
16	10	10	5	6	47	80

It is generally held that cases due to Type II pneumococcal infection are more severe and more resistant to treatment than cases due to Type I. While admitting this contention, we have not perceived, in the admittedly limited number of cases of each infection treated by us, any marked difference in the response to serum treatment, as we have obtained equally good results in both instances. Let it be strongly emphasized that we have abstained from serum treatment in all cases, irrespective of the pneumococcal type of infection, which were obviously mild and progressing in a favourable manner; moreover, we have never intervened later in the illness than on the sixth day. The results appear in the tabular analysis which follows, and illustrate the supreme importance of early treatment.

Analysis of Twenty-Six Treated Cases. Types I and II

Day Treated	Result		
	Aborted	Improved	Uninfluenced
Second... ..	6	—	—
Third	3	4	1
Fourth... ..	1	3	—
Fifth	—	3	1
Sixth	—	2	2

SYMPTOMATOLOGY OF SERUM-TREATED CASES

The effects of treatment by concentrated antipneumococcal serums may be conveniently summarized under two headings: (1) conspicuous immediate results; (2) characteristic general effects.

Conspicuous Immediate Results

Shock.—We noted in six of our twenty-six treated cases that the first dose of serum was followed by respiratory distress, varying from rapid and shallow breathing, with or without a sense of constriction in the lower chest or round the waist, to urgent dyspnoea and cyanosis, observed in two cases of the series. At the same time, the pulse became frequent and ill-sustained or for a short time barely perceptible at the wrist. The patient's face was livid, the lips colourless, and the eyes sunken. At this moment adrenaline was given, and was followed in every case by rapid cessation of the alarming symptoms. The onset of shock was from five to fifteen minutes after the serum injection; the phase of discomfort lasted up to half an hour if adrenaline was not administered.

Rigors.—In twelve cases a rigor or shivering attack followed the first injection, the highest level of temperature reached being 105.8° F. In ten cases, a rigor, with lower maxima, followed the second dose; in four only, the third or subsequent doses. Our experience consistently proves that a brisk rigor following the injection is of favourable import. This phenomenon was specially observed when the Parke Davis concentrate was used, and also with a particular batch of serum concentrate from the Wellcome Laboratories.

Sweating.—Profuse sweating, a constant accompaniment of spontaneous crisis in lobar pneumonia, does not occur with the same frequency when the clinical course of the disease is interrupted by serum treatment, nor is deferrescence, following a rigor, necessarily associated with sweating. Thus only six of our patients sweated after the first dose of serum and ten after the second. The presence or absence of sweating gave us no definite indication as to the probable course of the illness.

Cyanosis.—Cyanosis is a characteristic feature in almost every case of lobar pneumonia. Most clinicians believe that this bears no exact relationship to the extent of consolidation in the lung. Indeed, cyanosis is frequently observed long before consolidation has taken place. One of the most remarkable effects of the serum treatment is improvement in the patient's colour. Sometimes after the first dose, usually after the second, the normal complexion returns, so that one may perceive, even at a distance from the bedside, the disappearance of the pneumonic facies. This change often occurs before the pulse and respiration rates have subsided, and bears no relation to the physical signs of consolidation, which are usually better defined than before treatment, corresponding to the course of the inflammatory process in the lungs. We submit that there is considerable probability that cyanosis in lobar pneumonia is a toxic phenomenon due to damage to the alveolar walls by pneumococcal products; we claim this important evidence of the benign effect of serum treatment as proof of its highly specific action. An analysis of treated cases shows that cyanosis vanished in seventeen cases, was lessened in five, and remained unchanged in two cases which ended fatally. Two other cases were profoundly anaemic; therefore the characteristic cyanotic tinge was not to be expected. The respiration rate usually falls more gradually after serum treatment than after true crisis. More conspicuous is the disappearance of respiratory distress and cessation of the pneumonic grunt.

The Mental State.—Sleeplessness causes as much anxiety as any symptom of pneumonia to the physician in

attendance. Among other mental disturbances are restlessness and anxiety, with confusion of mind and even active delirium. The effects of serum are consistently beneficial in this respect, affording conspicuous relief to the patient. Natural deep sleep for some hours, without the aid of hypnotics, followed the first dose of serum in eleven of our patients, and in seventeen the mental state improved. Of the group of twenty-six cases, nineteen patients slept after the second dose and in twenty-two the mind became clear and composed. The exceptions were afforded by two fatal and two anaemic cases. Proof of the extreme deprivation of rest suffered in the untreated case of lobar pneumonia lies in the well-known fact that after natural crisis the patient will often sleep for days. No such exhaustion was apparent in our cases treated early; more than once, these patients have personally testified to their intense satisfaction in having enjoyed a night's good rest after the serum.

Albuminuria.—Among the consequences of the pneumonic toxæmia is albuminuria. Urinary tests were not made in every case, but in a number observed daily the disappearance of an albuminuria, often gross, was a constant sequel of treatment. In any event, one of the most frequent subordinate evidences of recovery from the acute stage of lobar pneumonia is diuresis; this flow is expedited by giving serum.

Characteristic General Effects of Serum Treatment

Whereas it is fair to state that the illness in cases of primary lobar pneumonia untreated by antipneumococcal serum becomes increasingly more serious up to the time of crisis, when within a few hours the picture changes, in cases treated early by the Felton concentrated antipneumococcal serum symptoms progressively abate after the inoculations. In cases in which treatment is begun later the effects are not dissimilar to those observed in normal subsidence by lysis. Slight irregular fever following a course of serum is not infrequent, this happening most often in cases treated late and in those in which scattered bronchitis accompanies the pneumonia. This slight fever, occurring when the height of the disease is past, must not be considered of adverse clinical significance or as evidence that the remedy is inadequate. Success or failure in the serum treatment of lobar pneumonia is to be gauged by the patient's improved general state, in particular by the disappearance of the so-called "toxaemic" symptoms rather than by slavish concentration on minor vagaries in his temperature. Analysis of the 26 treated cases shows that 11 became and remained afebrile following the last intravenous dose of serum, an irregular slight fever persisted for a few days in 12 others, while in 3 cases the temperature did not respond.

The pulmonary condition is not the only consideration in lobar pneumonia. At least an equal measure of attention must be paid to the heart and the general state of the patient. The importance of adequate rest has already been emphasized. We do not propose to digress into a discussion on the control of the pulse rate, although we incline to favour tincture of digitalis, given early in the illness, as a conservator of cardiac energy. We are not averse to the giving of alcohol (whisky or brandy) as required. Cane sugar or glucose may be taken freely, being a food which is easily assimilated and speedily utilized. Returning to serum treatment, this undoubtedly has favourable influence on the alimentary system. After the first, usually, almost invariably after the second, dose of serum, the tongue becomes moist and cleaner; appetite rapidly returns. It is hardly possible to describe the astonishment we felt on finding a patient who had suffered violent anaphylactic shock and a severe rigor, following serum administration at 11 o'clock in the forenoon,

sitting up in bed at 6 o'clock the same evening, when his final dose of serum was due, enjoying tea, bread-and-butter, and a boiled egg. This occurred on the fifth day of an illness which was exceptionally severe before treatment was begun. The inevitable loss of flesh and the asthenia which is a consequence of pneumonia are stayed or prevented if serum is given early in the disease, as on the one hand the illness is aborted and on the other the patient is not called upon to sustain the effects of days of fever and starvation. Hence convalescence is greatly shortened and assisted.

THE GENERAL EXPEDIENCY OF SERUM TREATMENT

It is appropriate to refer to certain essentially practical aspects of the results of serum treatment. Unquestionably lives are saved, the patient's sufferings are relieved, and the acute anxiety of his relatives is consequently soothed. Other more mundane considerations follow: admitting that the serum is at present costly both to make and to market, in all probability serum treatment represents actual economy. The services of both a day and a night nurse, essential for the case of severe pneumonia, may be dispensed with at an early stage; visits from the physician, twice daily or more often, soon cease to become necessary, and convalescence is so far accelerated that the wage-earner returns to work in a state of full efficiency, literally weeks before the untreated case. These considerations apply with equal force to the case of the sick in institutions and to the private patient; it would be exceedingly interesting to offset the expenditure on a course of serum treatment, say ten to fourteen guineas, with a virtual guarantee of speedy recovery, against the alternative cost of a long and serious illness, with prolonged convalescence, in the untreated case.

SERUM TREATMENT OF LOBAR PNEUMONIA COMPLICATING PREGNANCY

Pregnancy is occasionally complicated by lobar pneumonia, and miscarriage or abortion not infrequently ensues. Two pregnant women were treated by us. One was aged 27 years, with a recrudescence of nephritis, blood and much albumin (1.5 per cent.) in the urine, pregnant 2½ months; the other had a straightforward pregnancy of 7½ months. In neither case was the pregnancy disturbed, while the nephritic woman left hospital ten days later with only a "cloud" of albumin in the urine and no blood.

INFLUENCE OF SERUM TREATMENT ON THE PHYSICAL SIGNS

We deny, on the basis of our experience, that serum treatment causes delayed resolution of the consolidated lung. We are not entirely in agreement with those who assert that the course of events in the lungs is uninfluenced. Considering cases treated within the first three days from the onset, the physical signs, indicating the course of the inflammatory process in the lung, undergo rapid change, corresponding with the effect of serum in relieving symptoms. Signs of the first stage of resolution, weak or absent breath sounds, replacing bronchial breathing over the consolidated areas, and signs of the second stage—namely, the appearance of the coarse, moist rales found during resolution—follow on successive days, accompanied by rapid diminution of percussion dullness. Correspondingly, the typical viscid, blood-stained, rusty, highly albuminous sputum of early pneumonia, containing scanty alveolar and bronchial epithelial cells, changes in a day to a loose, purulent expectoration, full of polymorphocytes.

These rapid changes are to be likened, in our experience, to those which quickly succeed each other in the very mild cases of lobar pneumonia (albeit due to the pneumococcal Types I and II) occurring in adolescents and to infection

by unclassified strains of low virulence in adults. This class of case commonly ends by crisis on the third day of illness. An important difference exists between these mild cases and the typical severe cases in adult men and women selected by us for treatment—namely, that in the mild untreated cases physical signs are limited in extent. Ample evidence of the potential severity of our early cases was afforded by extensive consolidation of one lung, often accompanied by physical signs on the opposite side, which sometimes progressed, despite treatment, to an area of definite consolidation.

With few exceptions our patients, treated early, complained of pain, frequently at both bases, often referred to the shoulder or abdomen on the side where consolidation was most extensive; pleural friction was to be heard with the stethoscope. We noted a difference in this respect from the behaviour of untreated cases at the same stage of the disease, and suggest the following explanation. With alleviation of symptoms and restoration of lucid percep-

CASE 1.—Male, 38. Onset, sudden; symptoms, typical; signs, consolidation of whole right lower lobe, general bronchitis; dramatic improvement after first dose of serum; shock, absent; resolution rapid; pleural pain seventh day of disease.

tion, the patients undoubtedly become aware and grumble at lesser discomforts, which are ordinarily masked by the severity of the illness and the confused mental state usual at this stage. Moreover, it is not improbable that the pleurisy is arrested in the so-called "dry" stage before the gross "buttery" fibrinous exudate of late pneumonia has had time to develop. Movements of the chest wall are very limited on the affected side in pneumonia; the artificial arrest of inflammation by serum undoubtedly relieves this muscular spasm, and so permits a friction between the roughened surfaces of the visceral and parietal pleura. The condition lasts at most two to three days, and is relieved by local applications—a linseed poultice or antiphlogistine.

These points are worth noting. We became able, as our experience grew, to reassure our patients, saying that the symptoms were insignificant and would soon pass. We anticipate that the development of new symptoms and fresh physical signs, such as pleural friction on one or both sides of the chest, might well cause apprehension in the mind of the physician, treating his first case with serum, that complications or recrudescence of the pneumonia were pending. There is no cause for alarm.

LATE SERUM EFFECTS

Late effects from administration of therapeutic serums of whatever kind are apt to be disconcerting to the physician, and, particularly in the case of painful or swollen joints, distressing for the patient. Nettle-rash developed in two patients, both of whom had received the unconcentrated Type I antipneumococcal serum mentioned earlier in this paper. Adrenaline injections successfully controlled the irritation. Two patients had a transitory acute arthritis, yielding at once to salicylates—one after concentrated, the other after unconcentrated, serum.

COMPLICATIONS

It is impossible to give an opinion, on the slender basis of twenty-six cases, as to any alteration in the incidence of complications such as empyema, in cases treated by antipneumococcal concentrate. A study of the very extensive American literature on the subject suggests that serum treatment does not prevent these complications.

EXAMPLES OF SUCCESSFUL TREATMENT BY SERUM

We do not question that spontaneous recovery would have occurred, in all probability, in most of our successful cases, but we strongly urge that the remarkable amelioration in the patient's condition which follows serum is

CASE 2.—Male, 32. Onset, sudden; symptoms, severe; signs, consolidation of whole right lower lobe and later of left base; marked improvement after second dose of serum; shock, considerable; resolution satisfactory; pleural friction seventh day of illness.

more than sufficient justification for our advocacy of this treatment.

Considerations of space require the omission of full notes on representative cases; the reader's attention is directed to the charts, illustrating this paper, and to the accompanying legends.

A TYPICAL CASE TREATED BY NORMAL HORSE SERUM AS A "CONTROL"

A case of Type I infection, of average severity at the time of onset, was treated by normal horse serum as a "control" with the object of deciding the possible non-specific effects of horse-serum protein. A course of seven doses, given as usual in three doses of 20 c.c. and a final dose of 10 c.c., were given at twelve-hour intervals, beginning on the third day. The patient became steadily worse as his illness progressed unchecked. There was relapse, due to consolidation of the opposite lung, and when the illness ended by a slow lysis, extending over the seventh to ninth days, he was left extremely debilitated, and convalesced but slowly. In fact, physical signs of consolidation in both lungs still persisted three weeks after lysis.

UNSUCCESSFUL CASES

Much stress has been laid on the high mortality in cases of pneumonia with pneumococcal septicaemia. Blood cultures have been made by us in all our severest cases, but in none has there been a positive result. We offer no evidence on this point, but wish to emphasize that the observations made in this paper apply to the sporadic form of lobar pneumonia occurring in the British Isles. It is obvious that this form is far less severe than that which prevails in New York or that responsible for the Rand epidemics a few years ago. Likewise, the small number (26) of cases treated and the method of selection—namely, the choice of (1) early, or (2) severe cases—deprives our mortality experience of significance, for the group is not homogeneous.

There were three fatal cases. One patient (Type I) apparently recovered from his pneumonia with the aid of serum, but died from the results of a surgical operation (reported in the *Journal* of April 25th, p. 701). A second (Type II), our oldest patient, a man aged 60, did not respond to serum given on the fourth day of disease.

CASE 3.—Female, 21. Onset, sudden; symptoms, severe; signs, consolidation of whole right lung and later of left base; gradual improvement after second dose of serum; shock, absent; resolution satisfactory.

Outstanding adverse features were myocarditis, chronic bronchitis, past syphilis, and alcoholism. Death occurred on the fifth day, from heart failure rather than from the lung affection. In a third case (Type II), serum given on the third day of illness was followed by marked initial improvement; misled by this apparently good result, we unfortunately stopped treatment prematurely. The patient became worse. Serum administered after an interval of forty-eight hours was ineffective, and he died.

SUMMARY

1. The course of primary lobar pneumonia, due to the pneumococcal Types I and II, may generally be aborted if treatment with the homologous concentrated antipneumococcal serum is begun within the first three days of the disease.

2. The course of primary lobar pneumonia, due to Types I and II, may be favourably influenced if treatment with the concentrate is begun on the fourth or fifth day of the disease.

3. It is doubtful whether the course of the disease is influenced to any extent if treatment is begun later than the fifth day.

4. The contents of five phials or makers' doses, estimated to contain 10,000 standard antipneumococcal units per dose, generally suffice for early cases of Type I infection.

5. The optimum dosage for cases of Type II pneumococcal infection, and for later cases of Types I and II infection, is the contents of seven phials.

6. The intervals between doses should be not less than six hours, but may be conveniently extended to twelve hours if treatment is begun within the first three days of illness.

7. Unconcentrated antipneumococcal serums of high titre may be used with success for very early cases of moderate severity, and in adolescents.

8. The serum must be given intravenously; by no other route may satisfactory results be obtained.

9. Desensitization is unnecessary; 1 c.cm. of 1 in 1,000 adrenaline solution should be administered subcutaneously whenever symptoms of shock are apparent.

10. The intravenous administration of serum is especially effective in aborting and eliminating toxic phenomena, cyanosis, delirium, etc. The action of the serum appears to be specific.

CASE 4.—Male, 35. Onset, sudden; symptoms, typical but moderate; signs, consolidation of left base; improved after first dose of serum; disease aborted; resolution accelerated, almost complete on seventh day.

11. Considering the cases of Type I and Type II infection together, of 26 cases 18 were treated by antipneumococcal serums within the first four days of the disease. In 10 of these the pneumonia was aborted and in 7 improvement was apparent. One patient showed initial benefit, but relapsed and died. Eight were treated with serum on the fifth and sixth days; five were improved, and three uninfluenced. These results sufficiently illustrate the supreme importance of early treatment.

CONCLUSION

A final word of explanation of the form of this communication is perhaps desirable. It is a common mistake to claim too much for a new remedy; indeed, the field we have entered has been beset for years by enthusiastic advocates of a variety of medicaments. Good effects in two or three cases might be attributed to coincidence or to unconscious favourable selection, but any such influences may be excluded without misgiving when consecutive experience confirms first impressions. The accounts of treatment in America are widely scattered through the literature, and not easily accessible to most English readers. We pay homage to the workers across

the Atlantic and to those in Glasgow and Edinburgh, and pray to be excused detailed reference to the work of others; we do not wish to overload our text.

We have tried to convey to the practitioner a clear impression of what takes place at the bedside, and to guide him in dosage and in the treatment of emergencies. To those who are interested, we offer the advice to apply the remedy to the first suitable case that arises in their practice.

Memoranda

MEDICAL, SURGICAL, OBSTETRICAL

FRONTAL SINUSITIS WITH INTRACRANIAL SUPPURATION AND INVASION OF BLOOD AND CEREBRO-SPINAL FLUID BY DIFFERENT ORGANISMS

The following is a record of a case of acute frontal sinus suppuration terminating in meningitis, and presenting some unusual bacteriological features.

On April 25th, 1930, a male, aged 28, was admitted to the ear, nose, and throat department suffering from oedema of the left conjunctiva of three days' duration, limitation of eye movement, and proptosis.

On investigation there was definite tenderness over the left frontal sinus, and transillumination showed the left frontal area to be dark. X-ray examination disclosed little difference between the two sides. Next day a Howarth's operation was performed by Dr. J. S. Fraser; a little pus was present in the ethmoidal and left sphenoidal sinuses, but in the left frontal sinus there was a large quantity which, when tested, showed a *Staphylococcus aureus* infection. For three days after operation the temperature was high, and a growth of *Staphylococcus aureus* was obtained in a blood culture on April 29th. The next day abscesses appeared in the gluteal and deltoid regions. From the pus obtained by opening and draining these abscesses a *Staphylococcus aureus* was again cultured.

During the next fortnight the temperature continued to swing, and, on examination of the lungs, signs of old tuberculous lesions with definite cavities were found at both apices. The sputum contained no *B. tuberculosis*, but many organisms of the strepto-pneumococcal group. From blood culture on May 14th a very strongly haemolytic streptococcus was found. The patient improved to some extent, and blood culture a fortnight later was negative, although the temperature continued to swing. On June 4th he complained of headache and became mentally abnormal, refusing to speak but willing to do anything he was asked. The following day there developed paresis of the muscles below the left eyebrow and of the right arm. The knee-jerks were brisk and abdominal reflexes present. There was no ankle-clonus, but there was an extensor plantar reflex, a positive Kernig's sign, and some difficulty in swallowing. On lumbar puncture the cerebro-spinal fluid was turbid and under pressure, and a *Pneumococcus mucosus* was found. This was non-haemolytic, inulin-fermenting, bile-soluble, and agglutinated by Type III serum.

The patient died on June 6th. Post-mortem examination showed intradural and extradural abscesses over the left frontal lobe, with chronic osteomyelitis of the left frontal bone, and cario-necrosis of the roof of the orbit extending to the roof of the sphenoidal sinus. There was also an early well-marked leptomeningitis. On bacteriological examination of the pus from the intradural abscess two organisms were found—namely, a *Staphylococcus aureus* and a *Pneumococcus mucosus* (Type III).

The striking feature of this case is the variation of the type and origin of the infecting organism at different periods of the illness. In all, three distinct organisms were found—namely, *Staphylococcus aureus*, haemolytic streptococcus, and Type III pneumococcus. In the early stages a *Staphylococcus aureus* infection was predominant,

the source of this being presumably the infected frontal sinus. Later, however, a haemolytic streptococcal septicaemia developed, the organism probably having its origin in the lung condition. Unfortunately, a more complete examination of the sputum was not carried out, as at this time the significance of this source of blood infection was not fully realized. Finally, *Pneumococcus mucosus* was found in the intradural abscess along with *Staphylococcus aureus*, while the Type III pneumococcus was alone responsible for the infection of the cerebro-spinal fluid.

I wish to thank Dr. J. S. Fraser for his kind permission to use the case notes, and Dr. W. R. Logan for his guidance in the bacteriological work.

JOHN A. BURGESS, M.B., Ch.B.,
Assistant Bacteriologist, Royal
Infirmary, Edinburgh.

SPONTANEOUS PROLAPSE OF UMBILICAL CORD DURING EARLY MONTHS OF PREGNANCY

Spontaneous prolapse of the umbilical cord during the early months of pregnancy appears to be of sufficiently rare occurrence to justify a brief description of the following case.

Mrs. S., aged 37, engaged me to attend her at her confinement. She had had three children, the eldest being 16, and all previous confinements were normal. The patient had been under my care for about a month, receiving a course of intensive alkali treatment for gastric ulcer, and it was during the convalescent stages of this complaint that I made the routine ante-natal examination. All pelvic measurements were normal, and the uterus corresponded in size to a pregnancy of five months' duration. Foetal heart sounds could be heard quite distinctly, and, apart from a very slight degree of uterine prolapse, there were no abnormalities worthy of record.

A few days later I received a message from the patient requesting me to visit her immediately as "her inside had come down." Upon my arrival she explained that during the early hours of the morning she had discovered something protruding from the vagina, but had not experienced any symptoms suggestive of labour pains or abdominal discomfort of any description. There was a loop of normal pulsating cord, measuring about eight inches, protruding from the vagina, but apart from this the cervix would only admit the tip of the index finger. There were no uterine contractions.

It was evident that the only line of treatment to be adopted in this case was to encourage the early onset of labour. This was accomplished by the administration of continuous hot rectal saline, and pituitrin in 2.5 unit doses when pains threatened. Labour commenced about eighteen hours after the prolapse of the cord, and the subsequent history of the case was uneventful; the foetus and placenta were entirely free from abnormalities.

M. HAWKE, L.R.C.P., M.R.C.S.,
Tollesbury, Maldon. L.M.S.S.A.

Reports of Societies

OBSESSIONAL NEUROSIS

At the meeting of the Medical Society of Individual Psychology on May 14th, with the president, Dr. O. H. Woodcock in the chair, Dr. M. C. LUFF read a paper on a case of obsessional neurosis.

After a brief summary of the chief features of interest presented by the case, Dr. Luff considered these and other points in more detail. The patient was a married woman, aged 30. The obsessions of which she complained showed a close relation to schizophrenia. This finding suggested that in this case there was no clear demarcation between psychoneurosis and psychosis—a possibility which further study of the case served to confirm. Thus neither the fears from which she had suffered from the age of 7, nor