but a crudely empirical system of prophylaxis. The recent researches of Sir Ronald Ross and of Dr. Brownlee illustrate the importance of numerical epidemiology, and the final solution of the influenza problem will only be obtained by the harmonious co-operation of epidemiologists and bacteriologists.

REFERENCES.

- ¹Nothnagel's *Specielle Pathologie*, Band IV. Thiel I, pp. 1-195.
²Local Government Board Reports: C. 6387 (1891), and C. 7051 (1893).
³Creighton's *History of Epidemics in Britain*, vol. ii, p. 397. *Cf.* the evidence summarized by Greenwood and Thompson, *Proceedings Section of Epidemiology and State Medicine*, Royal Society of Medicine, April, 1918.

Preliminary Report

ON THE

INFLUENZA EPIDEMIC AT BRAMSHOTT IN
SEPTEMBER-OCTOBER, 1918.

BY

C. E. COOPER COLE, B.A., M.B.Tor.,

LIEUT.-COLONEL C.A.M.C.,

OFFICER IN CHARGE MEDICAL DIVISION, No. 12 CANADIAN GENERAL
HOSPITAL, BRAMSHOTT.

INTRODUCTORY NOTE

BY

COLONEL R. D. RUDOLF, C.B.E., M.D., F.R.C.P.,

Consulting Physician to the Canadian Forces in England.

COLONEL COLE and his officers have had a most extensive experience of influenza in the recent epidemic. The notes of the complications of the disease are very valuable—for example, the frequent rupture of the recti abdominales muscles. I have not been as much struck as the writer was by the fetor in the disease.

The frequency of relapses has been very noticeable; these relapses have often occurred several days (in one case ten days) after the temperature had originally returned to normal. Such relapses occurred while the patients were still in bed, and hence were not due to any chill or exhaustion.

The mortality of the cases admitted to hospital works out at 7.25 per cent., and of all the cases reported in the camp 3.6 per cent., which is noticeably higher than in the original epidemic of the spring, but low as compared to some reports of recent ravages. Death was practically always due to respiratory complications.

CHARACTER OF THE OUTBREAK.

After the outbreak of influenza in May and June our hospital had very occasional admissions of cases of this disease until the later part of September. On September 24th three cases reported, and on the succeeding days 9, 17, 24, 26, a maximum of 174 being reached on October 5th. Since then the epidemic has been abating, and on November 7th the total admissions for influenza were only 12.

In all, 2,247 cases have passed through hospital out of about 4,500 cases in the area; 163 cases had a fatal termination, the period of illness varying from five to twenty-seven days, and the pathological changes affecting the lungs or myocardium.

The usual history was of sudden onset of chilly feeling, headache, general aching, and weakness with dizziness; then cough and tightness in the chest, with glairy sputum, and very frequently epistaxis. Objectively an indescribable fetor was present in even the mildest cases, and, in the very severe, was almost overwhelming. It disappeared before complete recovery of the patient. The febrile course of the disease varied from twenty-four hours to fifteen days' continuous fever, running as high as 106.6°, inclined to be remittent, and ending by lysis. The types might be considered as:

(a) Mild, temperature becoming normal within three to seven days without disturbance of pulse or respiration. Considerable weakness persisted, and renal irritation was usually present. Even these mild cases showed a tendency to tachycardia on slight exertion in convalescence.

(b) The next grade of severity ran a course of five to twelve days with high fever, marked cyanosis or livid pallor, and rapid respiration—all evidences of severe

toxaemia, with very few signs in the chest except of diffuse emphysema or of bronchitis down to the capillary tubes, with sputum moderate to copious, glairy to muco-purulent to yellow-green purulent, and becoming dirty sanguineo-purulent to dark clotted blood. In some cases bright red blood was expectorated, as much as 4 oz. at a time; one case, for which no other cause could be found, proved fatal from haemoptysis. A number of these cases proved fatal, and showed peribronchial induration or patchy central bronchopneumonia.

(c) The most severe types were either (1) primary marked bronchitis with profound toxaemia, rapidly becoming pneumonic, or (2) a primary toxic type as in (b) above, the temperature falling to normal or thereabouts for one to six days and then rising again to a secondary severe pneumonic course, with a frequently fatal issue.

SPECIAL CLINICAL AND PATHOLOGICAL FEATURES.

Some peculiar clinical and pathological features were noticed in this series of cases. In the first place very marked fetor of the exhalations, so offensive in some cases as to render careful chest examination difficult, was pathognomonic.

The Respiratory Tract.

In the respiratory tract there was marked congestion from the nares to and through the pleura. The respiratory rate was frequently out of all proportion to pulse or temperature, fifty to the minute being often maintained for a week, with pulse not above 110. Rhinitis with epistaxis, often recurrent, was present in over one-third of the cases. Pharyngitis, tonsillitis, laryngitis, and tracheitis (often pseudo-membranous, causing dyspnoea, stridor, and inspiratory retraction of lower ribs), bronchitis, and bronchiolitis.

The cough was of several types—(1) explosive, (2) paroxysmal, closely resembling pertussis, and in a few cases was (3) "brassy." The bronchitis, at first dry, afterwards usually became moist with abundant muco-purulent sputum. The inflammatory condition extending deeper, lobular and pseudo-lobar pneumonia of variable extent developed. Fibrinous, sero-fibrinous and sero-purulent pleuritis occurred, 16 cases showing definite empyemata, streptococci more frequently than pneumococci on direct smear. Compensatory emphysema often developed out of proportion of areas of consolidation, and in 12 cases with severe chest signs interstitial emphysema developed in the mediastinum, and so extended up to the malar eminences and down over chest and abdomen. Only one such case recovered. Most of these cases showed definite small pulmonary abscesses either in continuity with the mediastinum or parietes. No cases of pneumothorax were observed. Areas of haemorrhage into the lung tissue were so often seen, in various stages from recent occurrence to liquefaction, that this condition might be considered almost pathognomonic of the disease. One very toxic case died from sudden onset of pulmonary oedema on the eighth day with very little consolidation. Several cases showed only "purulent bronchitis." Four cases showed activated pulmonary tuberculosis. Two of these became miliary, two miliary of the lungs, and one of the latter developed tuberculous basal meningitis.

Circulatory Effects.

The early cyanosis was toxic rather than asphyxial. The tongue itself was often of dark indigo and the whole body of a lilac tint for several days before death. Pulse usually relatively slow—for example, respirations 40, pulse 88, temperature 104°—and often dicrotic. The systolic blood pressure in previously healthy young adults often ran below 100 mm., and diastolic could hardly be estimated. In only one case was recent pericarditis found, and no recent endocarditis. The main change was myocardial, but rarely accompanied by right heart dilatation. The circulatory failure was often of very sudden onset, a pulse of 100 of good quality becoming 140 within two hours, and ceasing in less than four. The blood itself clots readily though purpuric eruptions were noted in some cases, as well as haemorrhages into the lungs and muscles. Phlebitis, brachial and saphenous, was not rare. There was usually a leucopenia, 2,400 to 9,000 white blood corpuscles per c.c.m. in purely toxic cases, and even in

extensive bronchopneumonia, but with pulmonary abscess formation, empyema, or other septic complications the count showed from 9,800 to 24,000. This leucocytosis or else the local reaction seemed to render the prognosis more favourable though not invariably so.

Blood cultures were negative, whether taken early or late.

The superficial and deep cervical and axillary lymph glands were almost constantly enlarged in severe cases. The peribronchial glands were much swollen, and occasionally almost broken down. The intestinal and mesenteric glands were not enlarged even in the cases with diarrhoeal symptoms. The spleen was rarely palpable, nor found enlarged *post mortem*.

Digestive Manifestations.

These were variable. There was the usual febrile mouth, with excess of slimy and most foul mucus. Anorexia, nausea, and vomiting were frequent, the latter usually exceedingly forcible, the vomitus consisting of large quantities of bright green fluid. Epigastric pain, with some rigidity, was a frequent complaint, and jaundice of considerable degree was usually of bad omen, fairly marked hepatic degeneration, and occasionally perihepatitis being found *post mortem*. Independent of purgation, several cases of profuse bloody diarrhoea and two of watery diarrhoea, with severe colic, occurred. Splenic and hepatic enlargement were rarely present. Abdominal distension was usually a late unfavourable sign. Lieut.-Colonel J. G. W. Johnson had to operate on five cases of influenza complicated by appendicitis, and found one gangrenous, one perforated, with abdomen full of cloudy fluid, and three acute catarrhal, with terminal inch of the appendix much congested. At autopsy many appendices showed peculiar bulbous terminal inch, with marked congestion of surface veins. In one case a mild serous effusion, and in several enterospasm, with slight ascites, was observed. No lesions were observed in the gross in the bowel wall.

Genito-urinary Signs.

Pain across the lumbar region was a common complaint, and in almost all febrile cases a mild nephritis developed—albuminuria, red and white blood corpuscles, and granular and hyaline casts being observed. In several cases the urine was distinctly bloody and decreased in quantity. Retention occurred in several, but not suppression. No renal oedema was observed. *Post mortem* many kidneys were acutely haemorrhagic, resembling scarlatinal nephritis. In over half a dozen cases there was swelling of the testicle and its coverings. One fatal case showed the coverings principally involved and gangrenous, streptococci present on cultures. The others cleared up without suppuration. There were over thirty cases of swelling of the parotid gland and capsule, occasionally bilateral, sometimes associated with the preceding. These were not clinically epidemic parotitis, but allowed free movement of the jaws, and the duct-mouths showed little change. One case supplicated. This complication occurred in one patient who had had mumps before.

Special Senses.

Hearing was very commonly dulled, and Captain J. A. Atkinson reported frequent occurrence of haemorrhage into the tympanic membrane. This occurred in some cases without pain, but in about forty there developed acute otitis, and one quarter of these had mastoid involvement. Four cases of frontal and ten of maxillary sinusitis were observed. Loss of sense of smell with fetid purulent nasal discharge and copious repeated epistaxis were observed. In several cases over twelve ounces of blood were lost at one bleeding, and packing had to be resorted to.

There was periorcular puffiness as in whooping-cough, with conjunctival injection going on to pus formation, and occasionally blepharitis was present.

Cuticular.

Very frequently a marked miliary sudaminal rash was present, occasionally patchy purpura, punctate erythema, jaundice and cyanosis, either turgid, livid, or ashy. One case showed purpuric blebs. Some very delicious cases showed marked tache cérébrale. Interstitial emphysema

occurred as described. Erysipelas of the face and the trunk with various local abscesses in the scalp, axilla, epitrochlear gland and thigh occurred, complicating the disease.

Joints and Muscles.

No definite joint lesions were observed, but arthralgia in knees and shoulders was complained of, while a rheumatic fever, a gonorrhoeal and a rheumatoid arthritis were lit up by the influenzal attack.

Myalgia and muscular weakness were very common symptoms. Abscesses were found in some muscles, and marked degeneration was repeatedly noted in the rectus abdominis. The muscle looked grey, cooked, and readily flaked, three hours after death. Often there was marked haemorrhage, as much as two ounces, into the sheath of the rectus, and the muscles themselves were frequently found spontaneously ruptured as cleanly as though cut with a knife. The haemorrhage was sometimes present throughout the length of the sheath from the costal cartilages to the pubis, though usually only in the lower quarter. Myocardial degeneration was frequently very obvious at section.

Nervous System.

Frontal headache and retro-ocular pain were of moderate severity. No breakbone pains were encountered. Pupils were normal and reflexes normal except knee-jerk, which was often difficult to elicit. Paraesthesia mild, involving the right leg, was noted in one case and a transient Bell's palsy in another. Sleeplessness from toxæmia, not air hunger, was a trying symptom. In cases with fever, even of short duration, a low muttering delirium, with tremor, subsultus, and carphologia, and occasional loss of control of organic reflexes, was frequently observed. Quite a number were very noisy and active in their delirium. Convulsions with cervical rigidity, opisthotonos and tetanoid spasms of hands and feet, occurred in several cases; only one recovered. The spinal fluid was clear and culture negative. No increased cell count was noted, except in two complicating cases—(a) a hemiplegia due to tuberculous basal meningitis, confirmed *post mortem*, and (b) a case with marked stupor which is now apparently convalescing, but which has repeatedly shown an increased cell count on puncture with as much as 80 per cent. lymphocytes, and on film on one occasion showed acid-fast bacilli. The brains, with the exception of one of these cases, have shown no gross change.

The pathological work quoted above was in the main done by Captain A. Montgomery of this hospital.

TREATMENT.

For purposes of treatment our patients were divided into three groups under Major Pope, Major Shannon, and myself. All patients were put to bed in moderately cool rooms at the earliest moment available, usually the fifth or sixth day of disease, and were not allowed up until the temperature had been normal for at least three days. In spite of this precaution one very mild case, whose chest had been negative, after a few hours up developed a massive lobular pneumonia with evidence of myocardial degeneration and died within forty-eight hours. Posture in bed was used to allay cough and also to promote expectoration.

Fluids only, and very freely, composed the diet, on a basis of four pints and four eggs to each sick man.

The initial purgative was in most cases calomel and Epsom salts, the latter to be repeated as necessary, often with very marked effects in lessening toxæmia. Simple enemata were also used and turpentine for distension, effectually. Local binders, mustard leaves and plasters, poultices and cups, were all used with relief of chest pain. For various types of cough balsamic inhalations were used as required, sedative and stimulant expectorant mixtures as indicated.

In some cases venesection relieved the toxæmia, especially if combined with (1) saline or (2) glucose and saline interstitially, intravenously, or by the rectum. Oxygen alone or through alcohol was helpful in some purulent bronchitic cases, either continuously through a Haldane apparatus, or intermittently by the open method, or subcutaneously.

The preliminary headache, general aching, and chilly feeling were relieved by phenacetin, aspirin and Dover's

powder, with hot drinks, in small doses. Groups of cases were put on—

1. Urotropin,	5. Sodium salicylate,
2. Quinine sulphate,	6. Salicin,
3. Salol,	7. Creosote and pot. iodide,
4. Tr. quinin. ammon.,	8. Oil of cinnamon.

These were all used in varying doses, and none were found to exercise any specific effect. Carbolic acid was not used owing to frequent renal irritation.

Serums—anti-diphtherial, pneumococcic, streptococcic, staphylococcic (the last three being polyvalent), also normal horse serum—were used, and seemed in some cases to reinforce the patient's resistance, but not to exert a specific effect.

Eusol has been tried intravenously in doses up to 250 c.cm., so far with uncertain benefit.

To reduce temperature: (1) Sponges tepid to cold, or alcohol rub if above 104°; (2) cold pack to neck and chest; (3) purgation and enemata; (4) aspirin, 5 grains for single dose, if not responding to the above.

Stimulants: Fresh air and oxygen, brandy or whisky up to an ounce every two hours, strychnine and atropine, strophanthin, various digitalis preparations, camphor in oil, pituitrin, and adrenalin, were each used, as indicated. Intravenous saline with or without glucose 25 per cent. was also used.

Sedatives: Cool sponging, chloralamide, ammonium bromide and chloral, veronal, codeine, heroin, hyoscine, morphine and atropine, pulv. ipecac. co.

From the multitude of agents employed their comparative futility is obvious. The line to follow in treatment is "primum non nocere," and the more expectant and symptomatic the course, the more satisfactory will be the result. This becomes particularly plain on observing a very large series of cases such as the present epidemic has afforded us. The natural variations in the course of the disease are legion; our influence on them is problematical.

PROGNOSIS.

Early cyanosis, high fever, and rapid respiratory rate are usually unfavourable symptoms, all being evidence of severe toxæmia. Relatively slow pulse-rate is not necessarily favourable, though a high rate is always ominous. Development of local septic foci promises favourably; leucocytosis is usually favourable. The delirium may be intense early in the case and completely disappear, the patient becoming perfectly rational and conscious of a sense of well-being, although still intensely cyanotic, and so dyspnoeic that he can hardly answer questions; in fact, this condition may go on to within a few minutes of dissolution. Bronchopneumonia is always serious, and, judging from *post-mortem* findings, carnification and scarring of the lungs, with probable bronchiectasis, will be sequelae inevitable in a great many cases.

POINTS IN THE TECHNIQUE EMPLOYED IN THE ISOLATION AND CULTIVATION OF ANAEROBIC BACTERIA.

BY

W. JAMES WILSON, M.D., D.Sc., D.P.H.,
BREVET MAJOR R.A.M.C.(T.F.),

AND

SERGEANT P. STEER, R.A.M.C.(T.F.).

(From the Laboratory of No. — General Hospital, R.E.F.)

As the isolation and cultivation of the anaerobic bacteria occurring in wounds present considerable difficulties, especially under active service conditions, a description of some methods that we have found useful may be of assistance to bacteriologists who have not yet evolved a technique of their own and are called upon to undertake the bacteriological control of the effects of serum and other treatment of gas gangrene, etc.

Media.

For fluid cultures we have obtained excellent results from brain broth, and brain broth with 1 per cent. of glucose, lactose, or saccharose. The addition of the sugars promotes rapid growth of the saccharolytic group of micro-

organisms, but the acid produced leads later to their destruction. For preserving cultures which can be worked out at leisure the plain brain broth is preferable.

It is prepared by adding to a litre of normal saline solution about 200 grams of chopped up brain substance. The medium is autoclaved in a flask and afterwards in tubes, each of the latter containing about 20 c.cm. of the broth and brain substance. In tubing it is convenient to pour the contents of the flask into a sterile dish, and with a sterile teaspoon to add the solid brain matter to the tube, and later to pour in about an equal volume of the more fluid part. If sugars are employed, acid fuchsin can be used as an indicator. These brain media can be kept indefinitely, and when inoculation is made deep down into the tube good growth of anaerobes will occur though the tubes have not been recently boiled, and though no attempt has been made to exclude air by the use of liquid paraffin. It is easy to remove material for film preparations, etc., by means of a long platinum wire, as there is no paraffin to necessitate the use of capillary pipettes.

Brain lactose broth is an excellent medium for the cultivation of streptococci. The effects of the growth products on the brain substance can be observed, *B. sporogenes* (Metchnikoff) causing a blackening, whilst *B. welchii* has no such effect. Von Hibler got as good results from the use of chopped up brain as he got from the use of chopped up muscle, but in this country the latter medium has been most extensively used.

For plate cultures we make most use of blood agar. We keep a stock bottle of sheep's blood always at hand.

The blood is preserved by the use of formalin and ether. A wide-mouthed bottle with a mark at the 1,000 c.cm. level has added to it 10 grams of sodium citrate dissolved in about 20 c.cm. of boiling distilled water. At the slaughter-house 1 litre of blood is received into the bottle, which is well shaken during the process. In the laboratory the uncoagulated blood is added through a sterile funnel to a bottle which has a tightly fitting cork. To 1 litre of blood 1½ c.cm. of formalin (40 per cent. formaldehyde) and 30 c.cm. of ether are added. The bottle is shaken, the stopper is tied in, and it is placed overnight in the incubator at 37° C. In making blood agar 3 c.cm. of the laked blood are added to every 100 c.cm. of melted agar, and the mixture is kept at 50° C. for half an hour to drive off the ether. The dilution annuls the antiseptic action of the trace of formaldehyde in the medium.

The blood agar prepared in this way is of a light brown shade and is fairly transparent. On being placed under anaerobic condition it becomes of a bright red hue. On this medium colonies of *B. welchii* are leaf-shaped; the centre of the colony is moist and more elevated than the flat, uneven margin. Colonies at the end of a week's incubation average 5 mm. in diameter. *B. sporogenes* (Metchnikoff) forms a spreading growth growing down into the medium, so that scraping the surface leaves the outline of the colony intact. *Vibrio septique* grows somewhat like *B. sporogenes* but does not invade the medium. *B. tetani* grows out from the main mass of the mixed growth as a very fine film with woolly margins. Tulloch has studied the effect of *B. sporogenes* in promoting the growth of *B. tetani* in fluid cultures. On the solid blood agar plate the cleavage products of *B. sporogenes* doubtless assist the growth of *B. tetani*, and as it spreads over the uninoculated part of the plate there is a fair chance of separating it from other anaerobes in the mixture.

If glucose is added to the blood agar the colonies of *B. welchii* are raised and opaque just like colonies of *Staphylococcus albus*. Litmus may be added as an indicator, but gets bleached under anaerobic conditions; on exposure to air the colour returns. We have found that *B. welchii*, *B. sporogenes*, etc., are able to grow on blood agar containing ½ per cent. of sodium taurocholate. This observation has facilitated the isolation of *B. welchii* from a mixture of other bacteria. The growth is not so luxuriant with as without the bile salt, but the presence of the bile salt tends to prevent confluence of the growth. Crystal violet in the proportion in which it is present in the Drigalski-Conradi medium, that is, 1 in 100,000, does not inhibit the growth of *B. sporogenes* on a lactose blood agar plate. The same plate heavily inoculated with *B. welchii* often yields only a very few colonies, but the colonies are large in size. There would appear to be a difference in their power to resist the antiseptic action of the dye, not only among different strains, but also among individuals of the same strain.

Symbiosis.

We have on several occasions isolated from wounds a Gram-negative cocco-bacillus which promotes the growth