REFRESHER COURSE FOR GENERAL PRACTITIONERS

WHOOPIING-COUGH

BY

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Whooping-cough is the most serious and fatal of the infectious diseases of infancy in this country, with the single exception of infantile gastro-enteritis. Almost two-thirds of the deaths occur in children under the age of 1 year, and of these more than half take place in the first six months. In the past ten years deaths have varied between 700 and 2,400 a year, and they generally exceed those of scarlet fever, diphtheria, and measles put together. The respiratory and possibly the nervous sequelae of whooping-cough still lead to long periods of invalidism.

Season and Age Incidence

Although the disease is more common in winter and spring, it is usually present throughout the year; and between epidemics, unlike measles, it rarely subsides to a very low level. The susceptibility of newborn infants to whooping-cough must be stressed. It has been estimated that not more than 25% of infants are born with circulating antibodies, that these disappear within a few months, and that they seldom or never give full immunity. In some infants under the age of 3 months the disease is mild, but many have dangerous cyanotic and even apnoeic attacks during a paroxysm, and these may be fatal from asphyxia or lead to anoxaemic convulsions. About 65% of children have whooping-cough before entering school.

In older children and adults an attack may be atypical and difficult to diagnose; owing to the size of the larynx

they do not whoop. Immunity is not necessarily permanent and second attacks occur, usually in adult life and occasionally in the parents or grandparents of children with whooping-cough.

Pathology

In its earlier stages whooping-cough is a superficial infection of the tracheal and bronchial mucous membrane with the small bacillus *Haemophilus pertussis*. In a few, mostly mild, cases the causal organism is an allied bacillus *H. parapertussis*.

A characteristic result of the infection is the formation of tough bronchial mucus. About the third week of the disease this mucus may be so viscid that it cannot be removed by the action of the cilia. It blocks some of the smaller bronchioles and so may cause collapse of small portions of the lung, with dilatation of the bronchiole above the block and compensatory emphysema of surrounding lung tissue. These small collapsed areas are usually situated in the base of one or both lower lobes. In some cases they involve complete segments of the lower lobes and of the middle lobe (right) and the lingual process (left), and may even involve the whole of one or more of these lobes (Figs. 1, 2, 3, and 4). While this collapse process is taking place the deeper layers of the bronchial walls become infiltrated with lymphocytes, and secondary infection may supervene, giving rise to infected collapse and bronchopneumonia. Bronchopneumonia in whooping-cough is nearly always associated with pulmonary collapse.

FIG. 1.—Girl aged 5½ years: 47th day of whooping-cough; ambulant; afebrile except for an occasional "spike" of temperature; respirations 24 to 28. Both cardiophrenic angles in the film are filled with dense shadow, indicating collapse in segments of both lower lobes. A lateral view showed some collapse also in the right middle lobe.

FIG. 2.—Boy aged 1½ years: 30th day of whooping-cough; afebrile when film taken, but with subsequent bouts of pyrexia; respirations 36 to 42. The right cardiophrenic angle (left side of picture) is filled with shadow, denoting segmental collapse in the right lower lobe. The left cardiophrenic angle is not clear-cut, suggesting small areas of collapse in the left lower lobe.

In the ordinary "uncomplicated" case of whooping-cough this process is of course minimal, but small areas of pulmonary collapse are commonly present even in ambulant and afebrile children with severe paroxysms after four to five weeks (Figs. 1 and 2). Perihilar and paratracheal glands may be moderately enlarged in whooping-cough, but not sufficiently to cause pulmonary collapse from external pressure on the bronchi.

The nervous system may be profoundly affected, though there are seldom any gross pathological changes. Minute scattered cerebral haemorrhages due to the mechanical strain of coughing are probably common, but usually symptomless. Occasionally they may be the cause of transient monoplegia, hemiplegia, or paraplegia. Haemorrhages are not the cause of convulsions in whooping-cough and are very rarely fatal; I have only

FIG. 3.—Girl aged 3 years: 26th day of whooping-cough: ambulant and afebrile except for occasional evening temperature of 99° F. (37.2° C.). The film shows right middle lobe collapse and also small shadows in the right cardiophrenic angle, suggesting some collapse in the right lower lobe.

once encountered death from cerebral haemorrhage. In patients dying of convulsions little is found in the nervous system beyond congestion and oedema. True encephalitis associated with whooping-cough is quite a rarity, but it may occur suddenly even in a mild case and leave serious sequelae.

Clinical Course

The average case gives little trouble until two to three weeks after onset of the cough, when severe paroxysms with vomiting may lead to loss of sleep, weight, and energy. Pulmonary collapse may begin about this time, especially in children under 5 years of age. The collapsed areas tend to become secondarily infected; the child then gets listless, the respiration rate increases, a cyanotic tinge may appear in the lips, and, if the temperature is taken night and morning, occasional "spikes" of pyrexia will be found. This condition may merge into bronchopneumonia, or bronchopneumonia may start suddenly from the second week onwards. On the other hand, mild and even abortive forms occur, especially in older children and adults and after immunization. Paroxysmal sneezing may partly replace the cough.

Complications

Bronchopneumonia is due to secondary infection with pneumococci, streptococci, staphylococci, or the influenza bacillus. During the past winter highly fatal cases of *H. influenzae* septicaemia have been occurring, associated with intractable bronchopneumonia and convulsions. *Convulsions* are probably the most common immediate cause of death. They are usually associated

FIG. 4.—Same case as in Fig. 3, same day. Right lateral view clearly showing collapse of right middle lobe and of the middle basic segment of the right lower lobe. The left posterior basic segment also seems to be collapsed.

with extensive bronchopneumonia and pulmonary collapse, especially in those cases which show poor or delayed response to antibiotic treatment.

Bronchiectasis is the sequela most to be feared. It is a potential risk in all cases in which pulmonary collapse is present. Many cases of bronchiectasis in schoolchildren have been traced to an attack of whooping-cough some years previously. Fortunately most cases of pulmonary collapse in whooping-cough clear up quite satisfactorily. The child who has a persistent cough for many weeks or months, who is subject to frequent recurrent respiratory acute infections, and who fails to thrive and become lively and active, should without delay be examined for pulmonary collapse and incipient bronchiectasis. The coexistence of measles and whooping-cough, both in the acute stage, is particularly apt to lead to these respiratory troubles.

The danger of *tuberculosis* following whooping-cough has been exaggerated in the past. The coexistence of whooping-cough with a primary complex may, however, be serious, especially in children under 2 years of age. This is the combination which produces occasional cases of acute miliary tuberculosis, with or without meningitis, and, perhaps more rarely, bronchial tuberculosis.

Haemorrhages resulting from the mechanical strain of coughing are rarely serious. The commonest is subconjunctival haemorrhage. Retinal haemorrhage is usually symptomless, but detachment of the retina has occurred. Cerebral haemorrhage has already been mentioned.

Hernia and prolapse of the rectum may occur in infants. The latter should be gently reduced each time without any lubricant. It seldom gives trouble after the cough subsides.

Nervous sequelae are just beginning to be recognized. They seem to occur particularly in cases which have recovered after exhibiting convulsions in the acute stage. Follow-up studies suggest that convulsions in subsequent illnesses, ataxia, optic atrophy, petit-mal seizures, and mental retardation may all be sequelae. Retrospective studies of the history of mentally defective schoolchildren have suggested whooping-cough as the starting point in certain instances, but this requires much further investigation.

Diagnosis

In a typical case the diagnosis is usually easily made on the history of a dry cough steadily developing and becoming paroxysmal, especially if there is a history of contact with a definite case, if the cough is worse at night, if sputum is coughed up and not swallowed, if the cough is followed by vomiting, if the child's face goes red in a paroxysm, or if there is ulceration of the fraenum of the tongue. But many attacks are mild and atypical, and laboratory tests are not yet 100% reliable.

In most cases, however, *H. pertussis* can be cultivated during the first three weeks of the disease: (1) by holding a fresh plate of Bordet's culture medium about 3 in. (7.5 cm.) from the patient's mouth during a paroxysm (cough plate method); and (2) by passing a fine pernasal swab along the floor of the nose to the nasopharynx just after a paroxysm (pernasal swab method). For these tests it is usually necessary to induce a paroxysm. To do this, place the thumb in the child's suprasternal notch, with the other hand extend the head *fully* and then flex it sharply, thus allowing the thumb to ride lightly over the child's trachea. If the child has not coughed for an hour or two this manoeuvre is usually immediately successful. The paroxysm so induced will generally make the diagnosis clear, but it may be confirmed, in some cases at least, by the use of the pernasal swab, which can be conveniently carried about. Unfortunately, a report may not be received for three to five days owing to the slow growth and small colonies of *H. pertussis*.

A blood count will almost invariably show a well-marked relative and absolute lymphocytosis by the second week of the disease, and often in the first week.

General Management

The average patient, who is virtually apyrexial, should not be left in bed. In good weather he should certainly be out of doors. The difficulty is the management of these cases in winter and during bad weather. Many can brave the elements with benefit. Others must be kept for weeks at a relatively uniform temperature indoors. It is essential to avoid so far as is possible secondary acute respiratory infections, and especially measles. All children should be encouraged to sit up during a paroxysm, should be supported, allowed to whoop as loud as they like, and trained to use a basin

for expectoration and vomit. Their lips should be wiped with damp swabs or tissue paper and these latter should preferably be burned.

Temperatures should be taken night and morning if there is the least suspicion that the child is not going on well. After the second week, occasional evening pyrexia, slightly raised respirations, cyanosis of the lips, and listlessness are suspicious signs demanding careful examination, including usually an x-ray film of the chest. This may entail sending the child by ambulance or private transport to an infectious diseases hospital. If bronchopneumonia develops, hospital treatment will often be required, for in whooping-cough it is a major illness.

If newborn infants contract the infection (a happening which should always be prevented if possible), and if they are threatened with apnoeic attacks in a paroxysm, it is desirable to send them to hospital with their mothers so that they can be breast-fed.

Treatment of Symptoms

There is no drug treatment which consistently produces dramatic improvement in whooping-cough. We can only hope to modify the course of the disease and prevent serious complications. This is more easily done in summer than in winter, when so many adverse factors such as cold damp weather, upper respiratory infections, influenza, measles, or pneumonia interfere with the action of a remedy, and lead to a return of coughing and vomiting.

Antispasmodics and Sedatives.—Bromoform drops, one for each year of age up to 6, or elixir bromoformi, $\frac{1}{2}$ to 2 dr. (1.75 to 7 ml.), or sodium bromide, codeine, or phenobarbitone are commonly used as sedatives. Ephedrine, $\frac{1}{4}$ to $\frac{1}{2}$ gr. (16 to 32 mg.) twice daily for an infant, and tincture of stramonium or of belladonna, 5 to 15 min. (0.3 to 0.9 ml.), have been much used in an attempt to relax spasm of the bronchial muscle. In small doses these drugs may do little more than irritate the stomach and may actually increase vomiting. Toxic doses will damp down the cough, but this degree of sedation is harmful. By reducing the force of the paroxysms these drugs may encourage the retention of mucus and pulmonary collapse. It is difficult to steer a middle course, and before prescribing such drugs each case should be considered on its merits. Phenobarbitone is probably as good a sedative as any, but it should not be prescribed in the presence of persistent cyanosis, or signs of pulmonary collapse or bronchopneumonia. In infants it may be given in doses of $\frac{1}{8}$ gr. (8 mg.) thrice daily. Elixir of luminal ($\frac{1}{4}$ gr. in one teaspoonful) is a convenient preparation. Atropine methylnitrate ("eumydrin"), which is used for dilating the pyloric sphincter in pyloric stenosis, can also be given as a sedative in 0.6% alcoholic solution, four to eight drops four-hourly. It has the advantage of not increasing vomiting and may sometimes relieve it.

Expectorants.—Ipecacuanha, ammonium carbonate, potassium iodide, and large doses of alkaline mixture for the older patients are all employed in what is often a vain endeavour to thin or dissolve the bronchial mucus. These drugs increase salivation and may induce vomiting. They are occasionally useful for the fourth week onwards, when the mucus is very viscid, but should not be prescribed as a routine or for long periods. They are hardly at all used in hospital.

The Decompression Chamber.—This treatment is the equivalent of an aeroplane flight at 12,000 feet for 45

minutes. It is suitable only for uncomplicated cases after the third week of the disease as an aid to clearing up severe paroxysms and stopping vomiting. It is contraindicated in pyrexial or pneumonic cases or those with cyanosis, but not in apyrexial cases with limited pulmonary collapse. It is being used experimentally at Park Hospital, London, and particulars can be obtained from the Emergency Bed Service.

Specific Treatment

Pertussis Vaccines.—I know of no convincing evidence that vaccines have any appreciable effect in the treatment of the ordinary case of whooping-cough in a child. They may have a place, however, as boosters of immunity in cases contracting whooping-cough after previous immunization, and possibly also in adults, as the latter are likely to possess some degree of basal immunity.

Chloramphenicol.—This is probably the best specific drug for whooping-cough, but its action is rarely dramatic. During the past winter, indeed, it has often proved disappointing. It is a very expensive drug and should not be wasted on mild or late cases or where an inadequate course is likely to be given. It should be given preferably before the twelfth day of the disease and only in cases which appear to be developing severe paroxysms. Subject to this, the earlier it is given the better. Usually some improvement in the cough is apparent about the fifth or sixth day of treatment. In ordinary dosage it does not kill but merely inhibits *H. pertussis*, and consequently a relapse may occur if the course is terminated much before the twenty-first day of disease. As a rule a ten-day course is indicated or, alternatively, a seven-day course followed by one of five days after a few days' interval. In children of 1 to 4 years administration is not easy owing to the bitter taste of the drug. Infants under 3 months are usually suitable cases for this drug unless the attack is very mild. Dosage is still uncertain. At present the following is suggested: four capsules (1 g.) a day for infants under 1 year; six capsules from age 1 to 3 years; and eight capsules daily from 3 to 10 years. These amounts should be given in divided doses at six- to eight-hour intervals. In hospital the nurses have little difficulty in giving the drug: they prefer the powder to be disguised in a sweetened or flavoured watery vehicle rather than a syrupy one. The child's nose may be gently held if necessary and the draught is then rapidly swallowed.

Treatment of Complications

For *bronchopneumonia* penicillin is indicated in high dosage, ranging from 100,000 units three-hourly to 500,000 units four-hourly. Severe cases may require to be admitted to hospital owing to the difficulty of treatment and the danger of convulsions. The oxygen tent should be employed wherever possible, and chloramphenicol may be required in addition to penicillin in resistant cases.

Convulsions are treated with soluble phenobarbitone intramuscularly or paraldehyde rectally or intramuscularly, but often with disappointing results.

Pulmonary Collapse.—If afebrile, the child should be up and about. Milder cases often clear up without special treatment. Resistant cases should be under the supervision of a specialist. Postural drainage should be encouraged over a Brompton frame, or equivalent double inclined plane, with the head downwards and 12

to 18 in. (30–45 cm.) below the level of the buttocks. Bronchoscopy may be required.

Prevention

Isolation.—A child with whooping-cough should be isolated so far as is possible from young children and especially from infants for at least the first five weeks of the disease. *H. pertussis* is not often cultivated from the bronchial secretions after three weeks from onset of the cough and hardly ever after five weeks. The duration of infectivity is therefore believed to extend to five weeks at the outside, even though the child may continue to have paroxysms of coughing and vomiting for six to ten weeks or more. It would seem that after the third week it is secondary infection which is mainly responsible for keeping up the bronchial irritation and the secretion of bronchial mucus that sets up the spasmodic cough reflex. There are many instances in which paroxysmal coughing and vomiting, after they have virtually ceased, are restarted by a fresh "cold" or other respiratory infection.

A newborn child should never be allowed to come into contact with any sibling or other person suffering from whooping-cough if it can possibly be avoided. Before the child is born or brought into such a household, the affected children should be sent away to hospital or elsewhere. This should be a routine precaution in the management of the puerperium.

While it may often be impossible to isolate a child with whooping-cough in a family of three or more children, the objective should be, if possible, to postpone whooping-cough till after 3 years of age. Return of the uncomplicated case to school may be considered safe after the fifth week from onset, but where paroxysms are still frequent or violent return to school may be delayed.

Immunization.—Pertussis vaccines for prophylaxis alone or combined with diphtheria A.P.T. have been the subject of extensive trials by the Medical Research Council in the last three years. The results will shortly be published. It is known that the incidence and severity of whooping-cough in the inoculated cases in these trials were appreciably less than in the controls, but that there was considerable variation in the results as between one vaccine and another, and even between different batches of the same vaccine. The best results were obtained with a vaccine not made commercially. Unfortunately it is much easier to make a bad pertussis vaccine than a good one. Until the processing has been improved there will inevitably be some disappointment in the results of whooping-cough immunization. But if whooping-cough is contracted within two years or so of immunization it will often be mild, and in some cases the attack will be prevented altogether or postponed to a less dangerous age. Immunization may be attempted at any time after the age of 2 months, but, as in diphtheria immunization, the earlier it is done the greater the need for an early boosting dose. A "booster" should be given after an interval of six to twelve months if immunization has been done within the first year of life. It is well to get immunizations over before the end of May in districts where poliomyelitis may occur. Whenever signs of epidemic prevalence of poliomyelitis appear, immunization against whooping-cough should at once be suspended until the incidence of poliomyelitis has fallen to a low level—that is, generally until the end of the year. Combined pertussis vaccine and A.P.T. should, in these circumstances, be particularly avoided.