BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 25 1941

ACUTE BRONCHIOLITIS IN CHILDREN

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(WITH SPECIAL PLATE)

"Capillary bronchitis may well be termed the essential lesion of influenza."—HORDER.

Capillary bronchitis, or, as it is better called, acute bronchiolitis, is not generally admitted to be a clinical or pathological entity. The pathologists, the paediatricians, and the writers on diseases of the chest for the most part deny it a separate existence. The general view is expressed by Norris and Landis (1938): "The latter term [i.e., capillary bronchitis] should never be used. While a lesion limited to the finer bronchioles is possible theoretically, practically it never exists alone, as an inflammatory process invading the swollen bronchi inevitably extends to the anatomically related and contiguous vesicles as well. The term 'bronchopneumonia' is much the most preferable designation, and by common consent is the one now in general use." It is difficult to share this view when one has, in an influenza epidemic, seen dyspnoeic and cyanosed children die in asphyxia. Holt and McIntosh (1933), for example, express a contrary opinion when, in an account of acute bronchiolitis in children, they write: "The symptoms, however, are due chiefly to a bronchitis which extends to the smallest tubes. Fibrinous exudate, and in some cases oedema, cause obstruction with great respiratory distress." Horder (1933), too, in the admirable article on influenza quoted above, writes: "But the dominant feature, rarely absent in any really severe case, is a condition of capillary bronchitis, with intense pulmonary congestion. This may be unilateral or bilateral, is more often basal than apical, but it is not seldom universal. This condition may well be termed the essential lesion of the disease, for even when actual consolidation of the lung is present this is quite often an incident by comparison, and if the patient dies he dies with the consolidation rather than of it."

In the catarrhal epidemic of January–March, 1940, the majority of patients escaped with an acute pharyngitis, but in many the larynx, the trachea, the bronchi, the bronchioles, or the alveoli were progressively involved. When the inflammation extended to the bronchioles dyspnoea and cyanosis became urgent symptoms, and although this phase was most obvious in babies and young children it was by no means absent in adult infections. Discussion here will, however, be limited to this condition of acute bronchiolitis in children, for in them it ranks as a first-class medical emergency.

The cases on which this paper is based were seen mainly in hospital practice. Fifty children were admitted to the Derbyshire Hospital for Sick Children with an acute respiratory infection during the first ten weeks of 1940. Twenty-seven of these were under the age of 1 year. Seven children died, all of them under the age of 2. Six other children were seen in family and consulting practice, and although these added little to the clinical picture they included two deaths in healthy middle-class children, aged respectively 4 and 2, and corrected the common impression that fatalities do not occur except in infants or in debilitated children. It is not suggested that all these children were suffering from acute bronchiolitis: in some of them the final diagnosis was acute bronchitis and in others bronchopneumonia, but in many it was possible to diagnose a phase in the infection when the small bronchioles were filled with exudate. Occasionally the children died in this phase of obstructive dyspnoea; some recovered without further extension of the inflammatory process, but more often the condition went on to bronchopneumonia, in three cases with a fatal termination some weeks later. No detailed case histories will be given, but a composite clinical picture of acute bronchiolitis will be attempted, and the treatment of the condition will be discussed in detail. In order that the clinical diagnosis may be substantiated the pathological appearance of the lungs in an infant who died in asphyxia will be described and illustrated.

Aetiology

Acute bronchiolitis is rarely seen except when influenza of a respiratory type is epidemic. It is not limited to any age group, but it is in children under the age of 2 years that its attack may be so often overwhelming, This may depend on a defective local resistance in the absence of any acquired immunity; often another factor appears to be the heightened virulence of an invading organism in its passage through several hosts, for the baby is usually the last member of the household to contract a catarrhal infection.

It is most often seen in children of the poorer classes, and here the lower immunity presumably depends on environmental factors: defective and injudicious feeding, confined living-space, and closer contact with infections. Middle-class children by no means escape, however, and the most rapid death in this series (thirty-six hours from the onset) was that of the son of a professional household whose nature and nurture were ideal.

No influenza-A virus was recovered by the Medical Research Council workers (C. H. Andrewes, in a personal

communication) during the 1940 epidemic, with the exception of one specimen brought back from the army in France. It will be remembered that Stuart-Harris, Andrewes, and Smith (1938) attempted a clinical differentiation of influenza, in which their virus was recoverable, from "febrile epidemic catarrhs," in which it was not. One of the clinical distinctions suggested was the much greater incidence of acute bronchiolitis in virus influenza. Further investigation has demonstrated that no such clinical differentiation is possible (Stuart-Harris, Smith, and Andrewes, 1940), since most of the clinical criteria, including acute bronchiolitis, occurred commonly in the non-virus epidemics of 1939 and 1940. Large numbers of throat swabs were examined by one of us (G. R. O.) in the 1940 epidemic, but the findings were too inconstant to assume that the epidemic was due to the organisms demonstrated by the usual methods of smear and culture. Pneumococci (not belonging to Group 1, 2, or 3), fusiform bacilli and spirochaetes of Vincent, Gram-negative diplococci of the *catarrhalis* group (later meningococci also), and streptococci (*viridans* and haemolytic) were the organisms most commonly found. The variable findings soon led to the belief that these swabs were only demonstrating secondary invaders. Unfortunately we did not succeed in getting a case within forty-eight hours of the onset to send washings for examination for virus. All cases coming to hospital had, after the onset, been sick outside for over two days.

Morbid Anatomy

The main features of the histopathology of influenzal virus infection in experimental animals are described in somewhat similar terms by the different investigators. Straub (1937) states that the primary lesion in mice infected with human influenza virus is a fibrinoid necrosis of the epithelium of the terminal and respiratory bronchioles leading to a state of complete epithelial desquamation. He gives a photomicrograph of an acellular fibrinoid plug in a bronchiole, and states that the exudation of polymorphonuclear leucocytes is not a feature unless secondary infection takes place. Other investigators do not refer to a "fibrinoid" exudate. Shope (1934) describes the bronchial exudate in ferrets infected with the swine influenzal virus as "a thick, tenacious, glassy, white mucous exudate which is usually profuse." He finds large numbers of inflammatory cells in the walls of alveoli, but the air sacs themselves contain coagulated plasma and very few cells. Shope and Francis (1936) find a similar picture in the lungs of swine infected with human influenza virus. The cut bronchi show a less abundant glassy, tenacious mucous exudate. There was epithelial damage and a pronounced peribronchial round-celled infiltration. The alveolar walls were much thickened, but there were few cells in the alveoli. Nelson and Oliphant (1939) studied the development of the lesions in mice infected with human virus. Like other observers they find the earliest lesion (eighteen to twenty-four hours) is damage to the bronchial epithelium, but there is an exudate in which polymorphonuclear leucocytes predominate. By forty-eight hours the polymorphs become necrotic and epithelial damage is more severe. The interstitial alveolar exudate appeared in three days, and this was the time the animals began to die.

The essential features of experimental influenza may therefore be summarized thus: (1) more or less complete destruction of bronchiolar epithelium; (2) obstruction of the lumen of bronchi and bronchioles by a plug of "thick, tenacious, glassy, white mucous exudate"; (3) peribronchiolar cellular infiltration extending to the interstitial tissue of some of the neighbouring alveoli; (4) alveolar sacs mostly free from exudate, but some close to affected bronchioles contain a serous exudate with few cells. These essential features were all present in the necropsies now to be described, and this is part of the justification for regarding them as truly influenzal.

During the 1940 epidemic in Derbyshire opportunities for post-mortem examination occurred in a number of cases. Two of these were especially interesting because they were almost pure acute bronchiolitis.

A boy aged 1 year and 7 months died in the Derbyshire Hospital for Sick Children; the necropsy was made on February 1, 1940. The pharynx and trachea showed simple reddening with no membrane and little exudate. The lungs were markedly emphysematous; they did not collapse when the chest was opened, but met in front of the heart. There was no pleural exudate. The cut surface of the lungs did not show any obvious pneumonic consolidation—the general emphysema gave the reverse appearance. Small pearly nodules very closely resembling miliary tubercles stood up all over the cut surface. They were not as numerous as in most cases of miliary tuberculosis; there were no tubercles elsewhere in the body, and acid-fast bacilli were absent. The nature of these "tubercles" is shown in the photomicrographs. Fig. 1 (see Plate) shows the lumen of a bronchiole 0.7 mm. in diameter. It is plugged with tenacious mucus in which only a few cells are present. The epithelial lining is completely necrotic and the wall is infiltrated with polymorphs, lymphocytes, and macrophages. Most of the alveoli near this bronchiole are overdistended with air, but in one part inflammatory changes have taken place; these are interstitial engorgement and infiltration and a serous exudate into the alveolar sacs. This mucous plugging and epithelial destruction was the typical lesion in the larger bronchioles; some contained rather more pus. Fig. 2 shows the changes in the smaller respiratory bronchioles. This bronchiole is seen to be plugged with a cellular exudate obviously different from the plug of mucus just described. The cells in the exudate are necrotic polymorphs with pyknotic nuclei and macrophages which are well preserved. Changes in the surrounding alveoli are similar to those shown in Fig. 1. A number of sections were examined after staining by Gram's method, but no organisms could be found. The remaining organs in this child showed nothing of interest.

Fig. 3 is from a woman aged 36. Necropsy was performed on February 29. The lungs were both markedly emphysematous and showed no pneumonic consolidation. The lesions were virtually the same as in the baby. This photomicrograph shows a small bronchus with cartilage. There is some necrosis of the lining epithelium, cellular infiltration is relatively slight, mucous glands are secreting freely, and the lumen is blocked by a plug of tenacious white mucus with very few inflammatory cells. The diagnosis before death in this case was influenzal bronchitis (not pneumonia), and dyspnoea and cyanosis were prominent features.

A third case may be mentioned because the patient, a man aged 50, died on February 21, 1940, less than an hour after an injection of morphine. His lungs were markedly emphysematous and met over the heart; the right weighed 19 oz. and the left 20 oz. There was no obvious pneumonic consolidation, but the bronchi were blocked by muco-purulent plugs. His other organs were healthy, but the heart weighed 16 oz. and showed early coronary arteriosclerosis.

The main difference between the lesions in these human cases and those in the experimental animals is the extent of the emphysema. Jackson (1934a) describes four types of bronchial obstruction by foreign bodies and exudates. In the "by-pass valve" ingress and egress of air are checked but not prevented, so there is no collapse or emphysema of the lung. In the "check-valve" type air can enter, but the egress is stopped, and this results in emphysema. The third type is a "stop-valve" which causes obstructive atelectasis. The fourth type is really a variant of the third type—a ball-valve obstruction allowing egress only, which results in rapid and complete atelectasis as in the "stop-valve" effect of Type 3.

In view of the great clinical importance of these plugs of mucus it would be interesting to know how they arise. Cartilage disappears from bronchi when they reach a diameter of about 1 mm.; the tubes smaller than this are known as bronchioles. Some state (e.g., Maximow and Bloom, 1934) that the mucous glands disappear with the cartilage. Others (e.g., Lewis and Stöhr, 1913) state that glands may extend beyond the cartilage and that goblet cells may be found until the ciliated columnar epithelium gives way to cuboidal and then respiratory epithelium. Miller (1940) states that cartilage disappears when the diameter reaches 0.6–0.7 mm. and that goblet cells become less as the diameter falls and disappear in bronchioles of about 0.4 mm. However this may be, it is notable that plugs of mucus are found in bronchioles much smaller than those which are said to have mucous glands. Was this mucus secreted by the epithelium before it was destroyed, or was it secreted by glands in larger bronchi?

Signs and Symptoms

The onset may be acute, with fever, very rapid and laboured breathing, cyanosis, severe cough, and prostration; but more often the child has for a day or two a slight temperature, pharyngeal cough, and some gastro-intestinal upset before the infection extends. The larynx may next be affected; the child develops a laryngeal cough together with soreness over the larynx, hoarseness of the voice, and sometimes aphonia. Dyspnoea and stridor, due to laryngeal spasm, may be present at this stage. From this phase the child may pass quite suddenly to bronchiolitis. The ultimate bronchioles become plugged with exudate and the clinical picture is dominated by *obstructive dyspnoea.* Respiratory distress is then very marked; the respiration rate is rapid—from 60 to 100 a minute. There is recession of the soft parts of the chest during inspiration. Cough is always incessant and disturbing. Cyanosis is often obvious quite early, but becomes extreme towards the end. Collapse is usually terminal, but sometimes the toxaemia appears to be profound from the start and the child is quickly apathetic and stuporous. The characteristic clinical picture is distressing and unforgettable: the head turning restlessly from side to side on the pillow, the dusky cyanosis of the lips and cheeks, the expression concentrated but unprotesting, the wildly distressed breathing, the relentless cough, and the final apathy. The physical signs are dominated by the presence of fine rales scattered over both lungs and, particularly towards the hila, mingled occasionally with coarser rales. The air entry is everywhere diminished, but there is no evidence of consolidation. The percussion note is more resonant than normal owing to the emphysema which is usually present. Sometimes sibili accompanying prolonged expiration may be heard, suggesting the presence of bronchiolar spasm. Occasionally large areas of collapse at the base may be suspected, presumably due to the blocking of large bronchioles with exudate. The degree of local emphysema or collapse presumably depends on whether the obstruction is of the "check-valve" or the "stop-valve" type.

The course varies considerably. A child acutely ill may be well and without symptoms in three days. Death from obstructive dyspnoea occurs, if at all, on the second, third, or fourth day. More often the fine rales give way to the coarse rales of an ordinary bronchitis when the acute phase is over, and this may persist for a few days. Sometimes consolidation develops and a protracted bronchopneumonia sets in; occasionally a whole lobe is consolidated. The recovery of the urgent and severe cases with obstructive dyspnoea appears to depend on the institution of the measures detailed below.

Treatment

A student examining the measures advised by a score of authorities for the treatment of acute bronchitis and bronchopneumonia in children will find opinions so various that he may doubt if a multitude of counsellors achieves wisdom He will discover that on such questions as fresh air, hydrotherapy, steam tents, oxygen, alcohol, digitalis, emetics, stimulants, mustard baths, plasters, poultices, venesection, blood transfusion, sedatives, and cough-mixtures there are as many opinions as authors. Abt (1939) represents mature opinion when he writes of the treatment of pneumonia in children: "We have long believed that one form of symptomatic treatment was as good as another provided neither form did harm."

One of the general methods to be adopted in the treatment of acute bronchiolitis is that these children should be nursed in warm moist air, with an adequate oxygen supply. In gamgee jackets, in antiphlogistine, and in linseed and mustard poultices it is difficult to put faith, but it is more difficult still to withstand the expectations of nurses and parents. Alcohol is the best sedative for children (and phenobarbitone the second-best). Brandy, whisky, or port may be used for children; doses may be individually determined, but 30 minims to 1 drachm two or three times in the twenty-four hours is an adequate dose for a child of 1 year. *No other sedative should be used for children with acute bronchiolitis, for if by sedatives their respiratory excursions are depressed and their coughs are quieted they die: any derivative of opium may bring a sleep which is final.*

"All bronchial therapy is futile," wrote the great Osler, dying of an influenzal infection; and this death-bed pronouncement has a papal quality. Moreover, there is to-day no need to resort for help to the Virginian prune, the wild lettuce, or ipecacuanha. Least of all to ipecacuanha: children are either not ill enough to justify the use of it in emetic doses or are too ill for this to be a wise therapy. In the treatment of acute bronchiolitis there are four factors demanding separate consideration—the infection, the obstructive dyspnoea, the cyanosis, and the collapse.

The Infection

It is important to use sulphapyridine (M & B 693) in full dosage, and to use it quickly. Infants 1 year old who are acutely ill when first seen should be given 1 gramme (2 tablets) immediately and 1/2 gramme four-hourly in the succeeding twenty-four hours. It is necessary to continue with the sulphapyridine tablets for at least a week in gradually decreasing doses, otherwise the infection will in many cases relapse and a protracted bronchopneumonia may develop. If it does so it becomes obvious in the second or third week that the sulphapyridine is having no influence on the course of the infection. It may be necessary to give the sulphapyridine by intramuscular injection; 3 c.cm. of the injection being mixed with 3 c.cm. of normal saline, and particular care being taken to inject direct into muscle. This is not easy in infants, who have little muscle and much subcutaneous fat. Large and slowly healing areas of necrosis are a common sequel of careless administration. It is rarely necessary to employ intramuscular injection: children are not usually disturbed by the ingestion of sulphapyridine. Alkalis or nicotinic acid are effective in relieving nausea and vomiting. This therapy rests on the assumption that the bronchial invaders are sensitive to sulphapyridine. Certainly there was no doubt of this in the last epidemic. The infection was quickly under control, and if the child could be maintained through its period of obstructive dyspnoea for a short time the sulphapyridine usually did the rest.

INDICATIONS FOR SULPHAPYRIDINE THERAPY

What are the indications for the use of sulphapyridine in the acute catarrhal infections of childhood? This is a question to which many different answers may be given: it will be generally agreed that there is seldom evidence in children, even with considerable dosage, of extreme depression of granulopoiesis. These are some empirical suggestions for its employment:

1. It should only be used if the infection appears to be severe enough to justify a week's therapy.

2. It should be used more often in epidemic than in sporadic cases, in weakly and debilitated children than in the healthy, in catarrhal infections complicating measles and whooping-cough than in primary infections.

3. It should always be used in infections with an acute onset—i.e., convulsions or rigors or high temperatures.

4. It may be more safely omitted in lobar pneumonia than in bronchopneumonia.

5. There is only need for its urgent administration in acute infections. In less severe infections a period of observation for the mobilization of the host's resources seems rational. It is easier to justify delay than the use of desultory or half-hearted measures.

The Obstructive Dyspnoea

This is the most urgent symptom, and *steam* usually brings great relief. The majority of modern writers will have none of it; others allow a kettle in the middle of the room at some distance from the bed; and a few permit a half-tent over the head of the bed. Steam-tents are the antithesis of the fresh-air treatment of pulmonary infections; but what proved virtue has fresh air besides its oxygen content? Those writers who believe that "fresh air has a stimulating effect on metabolism" are very careful to warn against air that is too fresh—i.e., a draught—and they temper their enthusiasm for alfresco therapy with warnings against the vagaries of the British climate. Moreover, where is this fresh air in an oxygen tent? There is no need to be afraid of surrounding the child with an atmosphere of steam: it is soon obvious that the patient's dyspnoea is relieved. The steam-kettle should be used with its nozzle inside the tent for periods of half an hour, and the child should be replaced in steam whenever breathing becomes difficult.

If there appears to be any bronchial spasm exaggerating the obstruction 2 minims of adrenaline (1 in 1,000) should be used and repeated. Otherwise, 1/150 grain of atropine, repeated four-hourly, seems helpful in decreasing the bronchiolar exudate.

We have no experience of bronchoscopic aspiration in this condition, nor any knowledge that it has been used in this country. Chevalier Jackson (1934b) writes thus of the kindred condition which he calls "self-drownage": "The accumulation may literally drown the patient in his own secretions. This is illustrated frequently in influenza and arachidic bronchitis. Infants cannot expectorate, and their cough reflex is exceedingly ineffective in raising secretion to the larynx. The cough reflex may be entirely absent in children. Age may be cited as one of the most frequent etiologic factors in the condition of self-drownage. Bronchoscopic aspiration is quite efficient, and can save any patient not affected with conditions that are fatal by other pathologic processes." Bronchoscopic aspiration under these conditions requires the services of an expert bronchoscopist who is accustomed to bronchoscopy in children without general anaesthesia.

The Cyanosis

Cyanosis is the indication for oxygen, which should be delivered through a Woulfe's bottle of warm water and a nasal catheter at the rate of three litres a minute for an infant (a rate of flow which is a continuous stream, making the water splash in the Woulfe's bottle). The nasal catheter is to be preferred to the small oxygen tent in acute bronchiolitis, for delivery by nasal catheter has the advantage that steam can be employed at the same time. The oxygen should be used continuously as long as the cyanosis persists and not, as is often recommended, for a few minutes every hour.

The Collapse

No measures devoted to preventing or relieving circulatory failure have the same importance as those already described. There is no drug which re-energizes the failing heart nor any which has a selective action in an overcharged venous system. Coramine is the drug which seems best to stimulate the failing circulatory system, and should be used for a child of 1 year by intramuscular injection in 0.5 c.cm. doses every four hours. Strychnine, adrenaline, camphor, digitalis, strophanthin, and eucortone all have their advocates. It is difficult to assess these last-minute remedies that are intended to arrest the patient's progress from the "saddle to the ground." Most often they appear to delay this progress rather than to check it finally; perhaps they are best regarded, in a friend's indulgent words, as "house-physicians' treatment." Some of them may be definitely harmful and are better avoided. Venesection is frequently recommended for right-sided heart failure; one paediatrician commends the withdrawal of "a drachm or two of blood from a vein as a most useful measure and one that is probably not employed often enough." It would certainly need to be used very often in this measure to make any difference to an overcharged circulation. Nothing less than the removal of 50 c.cm. would seem likely to give any relief to a child with a blood volume of more than twelve times this quantity. In cyanosed children with distended jugular veins it has definitely appeared to be of value, especially if the blood is removed rapidly from the circulation.

Summary and Conclusions

It is contended that acute bronchiolitis is the essential pulmonary lesion in epidemic influenza, as it is in experimental influenza. This condition is particularly common in young children, in whom it produces urgent dyspnoea and, if not vigorously treated, death by asphyxia.

The clinical picture and the morbid anatomy of the condition are described. It is suggested that the respiratory obstruction is caused by mucus in the bronchioles. The lungs of an infant showing this condition are described and illustrated.

Sulphapyridine, steam, and oxygen are the essential therapeutic measures. Bronchoscopic aspiration in the hands of the expert may be life-saving.

The use of any sedative demands especial watchfulness: opium or its derivatives bring swift disaster.

We are indebted to Dr. E. P. L. Hughes for permission to review some of his case notes and also to Detective-Sergeant J. S. Fayers for the photomicrographs.

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DOUGLAS HUBBLE AND G. R. OSBORN: ACUTE BRONCHIOLITIS IN CHILDREN

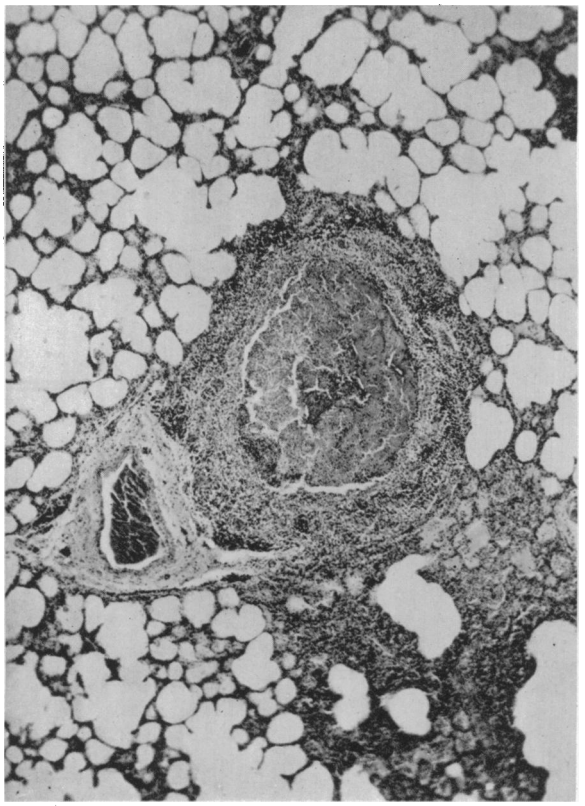


FIG. 1.—A bronchiole 0.7 mm. in diameter. Complete destruction of lining epithelium and plug of almost pure mucus, though there are no glands in the wall. General emphysema and localized alveolar changes well shown.

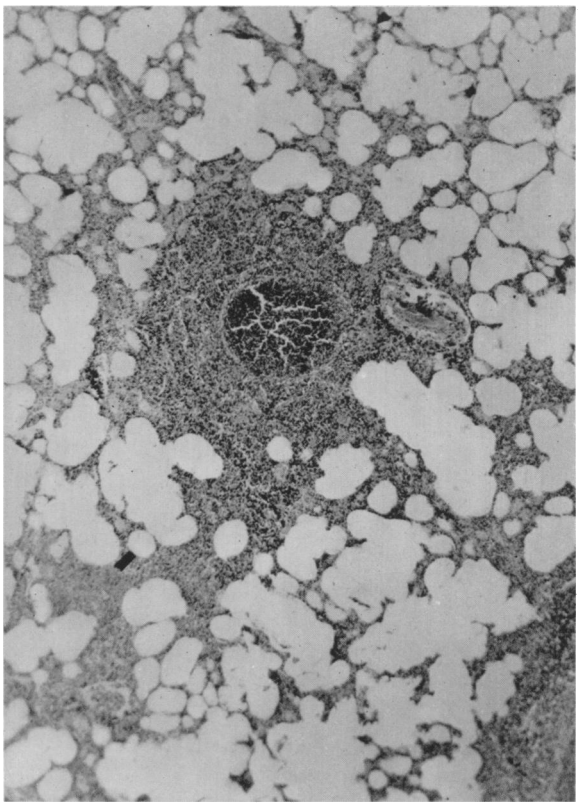


FIG. 2.—Respiratory bronchiole blocked by purulent plug. Peribronchiolitis, interstitial alveolar changes, and general emphysema.

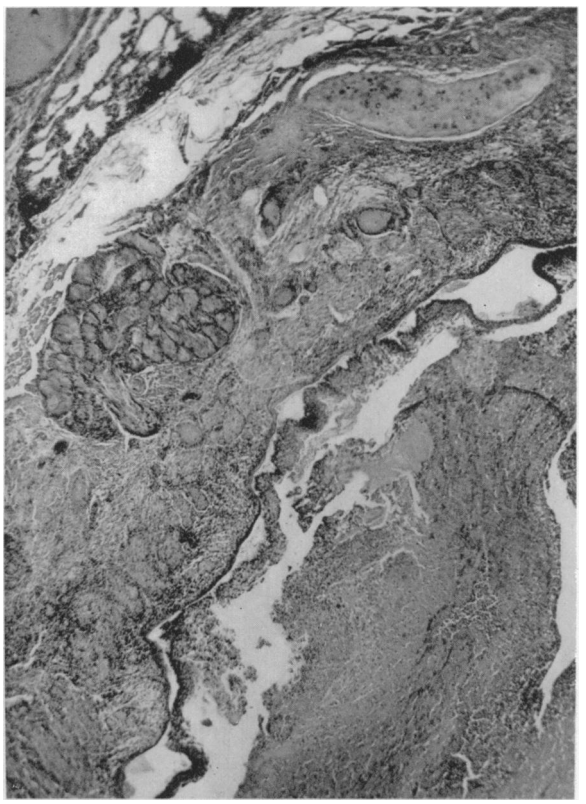
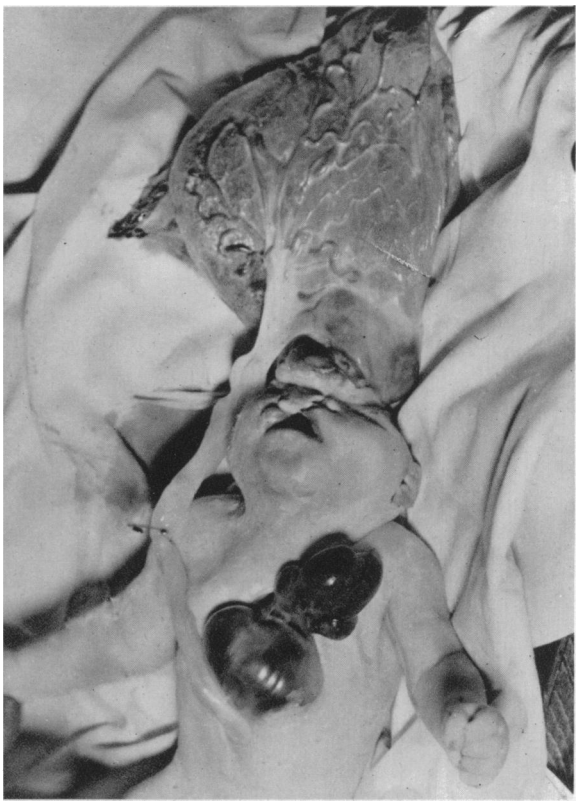


FIG. 3.—Small bronchus blocked by a mucous plug. Damage to lining epithelium and active secretion by mucous glands. Mucicarmine stain.

A. B. SLACK: MULTIPLE FOETAL ABNORMALITIES



Showing herniation of liver, heart, and brain, and cleft palate and bilateral harelip. Placenta adherent to brain.