haematogenous pulmonary tuberculosis lesions are always easily recognizable. This is also an assumption which I, after many years' experience of x-ray interpretation, cannot corroborate. Jacobs in a well-reasoned argument shows the unlikelihood that inhalation superinfection is a cause of pulmonary tuberculosis of the adult type. Yet it seems that close contact and crowding, favouring frequent and massive inhalation infections, are outstanding in the aetiology of the disease.

Two Possible Causative Factors

I think that two possible factors have not been taken sufficiently into account in the many arguments on this subject.

1. What is the effect of frequent doses of inhaled or ingested tubercle bacilli from without on the immunity balance between a host and the tubercle bacilli he already harbours? If these inhaled or ingested bacilli lodge on a mucous surface—and those in close contact with freely talking and coughing open cases must inhale and ingest large quantities of bacilli daily over long periods of time—they must be taken into the system, and if they do not themselves actually cause a new tuberculous lesion they must be destroyed. In their destruction the protein moiety of the bacillus, to which all infected persons are sensitive, will be liberated and must have an effect on the host of exactly the same quality as that of a dose of tuberculin. If such doses of the protein moiety of the tubercle bacillus are frequent and large, some disturbance of the immunity balance in one direction or another is inevitable. An adverse disturbance, if of any great degree or of an appreciable duration of time, should influence the behaviour of the tubercle bacilli lying dormant and clinically inactive in the lymphatic system or elsewhere of all infected persons. I say "elsewhere" with reason, for all are familiar with the small tuberculous focus in the lung which remains unchanged in size for years and yet is seen to be the possible starting-point of a spreading granuloma at some later date.

2. The last barrier between the lymphatic system (which in all Mantoux-positive individuals harbours tubercle bacilli) and the blood stream is the bronchial gland system. Once past these glands the lymph flows unimpeded into the blood stream via the lymphatic duct. Krause's experiments in guinea-pigs show that tubercle bacilli, whatever the site of entry into the body, unless arrested on their travels will always percolate the lymphatic system centripetally, finishing with involvement of the bronchial glands; and, further, that it is not until the bronchial glands have been involved that dissemination to other organs occurs. If the site of entry is the muscles of the leg it will obviously take the bacilli longer to reach the bronchial glands than when the site of entry is the bronchial mucosa, and if the site of entry is the intestinal mucosa they will take an intermediate time. The size of dose and the virulence of the bacilli will also influence their rate of travel. Furthermore, the further they have to travel the greater the number of glands or filters they have to pass and the greater the chances of their being temporarily or permanently arrested on their journey.

In those persons whose bronchial glands contain tubercle bacilli it is not hard to suppose that an adverse disturbance of the immunity balance caused by repeated ingestions of non-lesion-producing tubercle bacilli from an outside source might result in increased activity of the resident bacilli and a seepage of them into the lymphatic duct and thence to the blood stream.

It is not necessary to suppose that tubercle bacilli in the blood stream will always produce widespread generalized military tuberculosis: we are all familiar with localized miliary-type infection. Generalized military tuberculosis, a comparatively rare event, surely presupposes a gross bacillaemia. The body, especially of the Mantoux-positive, is relatively tolerant of the tubercle bacillus, and in the event of a small entry into the blood stream it is quite possible that such bacilli, when deposited in small numbers in the lung tissues (the lung being the first capillary system they will encounter), may cause no lesion and be destroyed, or if not destroyed may only produce a minimal "secondary" and a non-progressive granuloma, in which they may ensconce themselves for hibernation. Others, again, may be deposited in larger numbers or be more vigorous and be the starting-point of the usual spreading granuloma.

Our knowledge of the rate of flow of the blood in the different parts of the lungs is scanty, but in view of the fact that in

normal breathing only the lower halves of the lower lobes are used it is quite possible that without the mechanical acceleration of lung inflation and deflation the blood flow is relatively more sluggish in the upper lobes. This would favour the deposit there of blood-borne bacilli and would fit in with the preponderance of initial lesions, and of new lesions in those already diseased, in these areas. To quote again from Bannen, the fact that most people sleep on their right side, which further restricts the movement of the right hemithorax, might possibly be used as another argument for this being the commonest site for new haematogenous lesions.

A Hypothetical Answer

A hypothetical answer to the questions would then read as follows: Pulmonary tuberculosis of the adult type is found in those persons who have been previously infected and is favoured by close contact with persons who are excreting tubercle bacilli. It is in these cases an exogenous superinfection. It is improbable that the initial lung lesions are caused directly by the inhaled tubercle bacilli. It is possible that these lesions, and new lesions in quiescent cases, may be caused by (a) bacilli which come to the lung in the blood stream from foci of living bacilli already in the lymphatic system, or (b) bacilli dormant in minimal and unrecognized lung lesions, whose activity in both cases has been increased by frequent massive ingestion into the system of tubercle bacilli from without whose destruction in the body liberates unknown quantities of the protein moiety of the bacillus to which the infected person is sensitive. That is to say, exogenous superinfection causes endogenous exacerbation.

This may appear a complicated hypothesis; but if a simple explanation fails, complexity is unavoidable. I put it forward as a possible hypothesis, not claiming that it is a satisfactory one, that it is true, or even that it excludes others; but as a basis for further study of this fundamentally important subject.

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OEDEMA OF THE GLOTTIS COMPLICATING MEASLES

A REVIEW OF EIGHT PERSONAL CASES

BY

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The recent account in the *Journal* (March 7, p. 325) of 4 cases of coincidental association of measles and laryngeal diphtheria prompts me to place on record the following brief summary of 8 cases of oedema of the glottis complicating measles. It is doubtful whether the possibility of this complication occurring save as a rare eventuality is generally recognized, as most textbooks of medicine and surgery do not include measles in the list of causative factors of oedema of the glottis, nor, in the general sections where reference to the complication may be made, is there anything to indicate that it is more common than such rare abnormalities as abscess of the brain, optic atrophy, or peroneal muscular dystrophy. Measles is as remarkable in the constancy of certain of its features as in the variation, in successive epidemics, of the dominant complication. Thus, bronchopneumonia, mastoid infection, and enterocolitis are common events which may take their turn in this fashion, and less frequently so may oedema of the glottis.

Clinical History of the Cases

In the widespread and severe outbreak of the winter of 1929-30, while in practice, my colleagues and I attended some 950 cases of measles. Of this number about two-thirds were moderately to severely ill, and included 186 cases of bronchopneumonia, 48 of them fatal; but the outstanding circumstance

of the infection was the occurrence of 8 cases of oedema of the glottis with 6 deaths, the 2 recoveries comprising one patient who managed to survive without operation and one who recovered after tracheotomy. Of the 6 fatalities, one took place so rapidly that death occurred within less than 20 minutes of the apparent onset of the respiratory distress, and one was in a child whose parents had agreed to send it into hospital but subsequently changed their mind (the case being "only measles") without making further arrangements; the remainder took place in hospital—three on the night of admission and one the following night. Tracheotomy was not performed in any of the fatal cases—in the first two instances because this was rendered impossible by the march of events, in the other four because temporizing measures were instituted, the condition being diagnosed as laryngeal diphtheria and the respiratory distress thought not to be of immediate urgency.

Attention was sharply focused on the possibility that oedema of the glottis was the factor responsible for the development of the laryngeal obstruction in the second case of the series. This happened to be the younger brother of the first, and he chanced to succumb in identical manner. The elder brother had had a moderate attack of measles with no untoward features until 2 days after the appearance of the rash, when the cough became croupy and some slow dyspnoea and difficulty in swallowing became noticeable. On examination there was no evidence of diphtheria in the throat, no tonsillitis, and no cervical adenitis, but the pharyngeal tissues seemed rather swollen. The boy was transferred to hospital in the late afternoon and died suddenly from acute laryngeal obstruction about 10 o'clock the same evening. The younger brother showed the rash 18 days later, developed stridor and difficulty in swallowing after an interval of 2 days, was transferred to hospital, and died from asphyxia almost at the same hour as had his brother.

Such a striking similarity between the two cases could hardly have been produced by the coincidental association of two unrelated diseases with totally dissimilar incubation periods, but cogitation on the subject was rudely terminated the next day when I was called to the case of a girl of 4 years, who was dead on arrival. The request unhappily had been conveyed by foot messenger, and, although attended to at once, vital moments had been lost. The whole episode, it was possible later to ascertain, had lasted less than 20 minutes, and the mother had not thought of calling in aid until some 10 of these had passed. There had, however, been certain premonitory symptoms, which had not attracted much attention. The fourth patient was the child of those parents who changed their mind about hospital treatment and later were unable to obtain medical aid in time. The fifth recovered after tracheotomy, the sixth died without it, and the seventh recovered slowly without operation after an anxious period of 12 hours. In the last-named instance the obstruction had come on gradually during the night following the appearance of the rash, and had reached its peak about 2 hours before the child was seen. At that time obvious respiratory embarrassment, duskiness, quiet stridor, and laboured breathing were apparent, and there was a troublesome short thick croupy croak, due seemingly to inability to dispose of spittle accumulated in the back of the throat. As the hour was still early it was decided to remain on the spot for a time; after the passage of a couple of hours it became evident that the condition was no worse and might have been a trifle better. As the patient lived only a short distance from the surgery it was arranged that the parent should keep a close watch on the patient's state and at once notify any change. But 4 hours later respiratory effort had become less strenuous and was followed by progressive improvement, although the duskiness was not relieved for a further 8 or 9 hours. Subsequent recovery was uneventful.

The eighth and last case in the series was the most instructive, as it was possible to secure conclusive proof of the nature of the laryngeal disorder. The patient, a girl aged 2, developed difficulty in breathing 5 days after the rash had made its appearance. She was taken by car to the general hospital, where she was seen by the E.N.T. specialist (now deceased), who diagnosed laryngeal diphtheria in spite of all persuasion to the contrary. The child was thereupon transferred to the infectious diseases hospital, where it died later without having had a tracheotomy

performed. Death was certified as being due to laryngeal diphtheria and measles. With the parents' permission, however, the coffin was unsealed and the larynx removed, when examination disclosed almost total obliteration of the airway due to oedema and not a shred of membrane!

Other Series of Cases

As is to be expected, similar incidents were experienced simultaneously in other parts of the country. Thus in one small institution in a provincial town there were 6 deaths from this cause within a few weeks, and it has been possible to ascertain that each case had developed characteristic premonitory symptoms, the significance of which was not appreciated, and all these patients died rapidly within a matter of minutes from sudden laryngeal obstruction. The premonitory period had varied between 3 and 6 hours, a finding in complete agreement with that of the present series. The operative mechanism, however, had not been manifest to those in charge, so that towards the end considerable alarm had been occasioned as the children successively choked to death. In London, three medical acquaintances had between them 4 such cases, with one other, which may have been doubtful, as there had been diphtheria in the house about a fortnight previously. And so, no doubt, could instances be gathered from all parts of the country if this were desired. In all the above cases, a total of 18, it may be added that pharyngeal swabs were taken in 12 and examination for K.L.B. proved consistently negative.

Diagnosis

It is of some importance, apart from the desirability of accurate diagnosis, to differentiate between oedema of the glottis complicating measles and laryngeal diphtheria occurring in association with the disease, because failure to do so may result in loss of life. The main reason for this calamity probably arises from the fact that the premonitory features of obstruction in oedematous laryngitis are much less suggestive of impending closure than in laryngeal diphtheria, the process being insidiously progressive almost to the final point when suffocation rapidly and violently ensues. In diphtheria there is seldom need for extreme urgency. The condition may often be diagnosed by ear on the doorstep, by the nose on the stairs, and by a glance in the patient's room. The noisy stridor, the marked croupy cough, the vigorous paroxysms of suffocative dyspnoea, are features which early constrain attention and should ensure timely measures. The reason for this fundamental distinction is not obscure, and lies in the different character of the responsible morbid processes. In diphtheria the interior of the larynx becomes filled with membrane, which often spreads over the cords and downwards into the trachea. Irritative and obstructive phenomena are therefore early features and provide fair warning of what is to be expected. The formation of membrane is a gradual process, and so, too, is the obstruction, apart from the croupy paroxysms or suffocative spasm due to detachment of a portion of membrane. Except, therefore, in neglected cases or in infants, extreme urgency in membranous croup is a rare event and tracheotomy is seldom done *au grand galop*.

In oedema of the glottis, however, the position is quite different. In the first place, the vocal cords are little affected owing to the close attachment of the mucous membrane to the underlying cartilage. Stridor therefore is not marked as an early feature and probably does not occur until the oedematous process is well under way. Secondly, the swelling is most pronounced in the lax tissues of the upper aperture of the larynx, giving rise fairly constantly to two early clinical items—namely, difficulty in swallowing, produced by the oedematous infiltration of the epiglottis and attendant aryepiglottic folds which mechanically hinders the initiation of the swallowing act, and slow laboured dyspnoea due to narrowing of the air channel. Thirdly, the infiltrative process, although regular in its progression to a crisis generally within a period of 2 to 6 hours, when fatal obstruction may supervene, is not accompanied by concomitant prognostics, so that the gravity of the situation may not be patent. Thus it may be appreciated that oedema of the glottis in measles, with its subtle onset and insidious development, when confused with laryngeal diphtheria

may well tempt the clinician to hazard conservative measures, with most serious consequences unless immediate relief is at hand.

Summary of Conclusions

It may be of service, therefore, to summarize the features of oedema of the glottis complicating measles and to emphasize a few points which may help to distinguish it from laryngeal diphtheria:

Its occurrence may be a feature of certain epidemics, when the incidence is probably under 1%.

The process tends to make its appearance after the rash, most commonly about 2 days later, although there are instances of its developing as early as the first day and as late as the fifth day.

It is not necessarily associated with a prodromal laryngeal catarrh, although laryngitis was a feature of the epidemic relating to the present series.

Premonitory symptoms are constantly present for a period of 2 to 6 hours. They consist mainly of croupy cough, subdued stridor, slow dyspnoea, and difficulty in swallowing. They are progressive, but, in contradistinction to laryngeal diphtheria, are not concomitantly indicative of the degree of laryngeal occlusion, so that the grave nature of the affection may be overlooked. Once the obstruction becomes marked, fatal asphyxia rapidly ensues, often within 20 minutes. One case, however, recovered spontaneously, and one succumbed after an apparent improvement lasting 24 hours.

In a doubtful case diagnosis may be made by opening the child's mouth and sticking a finger down the throat, when the swollen epiglottis and aryepiglottic folds can be quite easily felt.

Indications of diphtheria will generally be absent; but the possible association of faucial disease should not dispose the clinician to temporize if the laryngeal symptoms have made their appearance within the few days following the eruption and present the above-mentioned characteristic features.

The mortality in untreated cases is probably not far short of 100%. Thus, in 8 cases of the present series there was only one spontaneous recovery, and in 10 other undoubted cases there were none.

Oedema of the glottis complicating measles is not an academic curiosity but a vital entity which may confront the practitioner at any time during an outbreak of the disease.

Medical Memoranda

Full-term Extra-uterine Pregnancy with Living Child

For the sake of record and to emphasize a method of treatment, I have been urged to write this case report and to refer briefly to three others.

CASE RECORD

The patient, a 7-para aged 39, was admitted to Mackay Memorial Hospital, Taihoku, Formosa, on March 1, 1931, in an exhausted condition, with a history of "having been in labour" three days. The radial pulse could not be felt. The pulse was 55, respiration 38, temperature 35.2° C. (95.4° F.). There was a history of severe abdominal pain for three days, with blood discharge from the vagina; she was constipated during this period. The movements of the child could still be felt by the mother. The last menstrual period had occurred from April 13 to 15, 1930. In June and in September she had had attacks of abdominal pain which kept her in bed a few days, and according to the husband there was no vaginal bleeding at these times. From January 5 to 15, 1931, and from February 27 to March 1 she had had further attacks of pain which doubled her up, the pain at the final attack being the most severe of all. On vaginal examination the cervix could not be felt; by abdominal examination the foetal parts were unusually easily palpated and seemed to be just under the skin. A diagnosis of full-term extra-uterine pregnancy was made and immediate laparotomy undertaken.

The secondary gestation sac was filled with a greenish-yellow fluid and had adherent omentum and gut over a wide area. The cord was ligated and divided, and the child delivered. The placenta was firmly adherent to the left side of the posterior wall of the abdomen, extending down to the

uterus, which could be felt drawn up and to the left, small and firm; the placenta was also adherent to the small gut, which was distended, red, and velvety. There was no haemorrhage in the sac or in the peritoneal cavity. The patient died fifteen hours later from ileus and shock. As there was no time to investigate the exact relations of placenta and uterus at the operation, the husband gave permission for a limited post-mortem examination on condition of his being present. This was carried out in the operating theatre, and the following is a copy of my notes made at the time: "Post-mortem examination 10.20 a.m. in operating theatre, husband and his sister present. Operation wound opened up; there was no blood in the sac or in the peritoneal cavity. Placenta adherent and involved the left side of abdomen and left side of uterine fundus; could not palpate adnexa of right side. Without further cutting could not free placenta or see pelvic contents. Husband, a very sane man, considering we had found out what was necessary, did not want her cut any further."

The child was a well-formed healthy girl weighing over 7 lb. (the chart did not record the weight, but I have distinct memory of her being well over normal weight). Her subsequent history showed that she was not only a beautiful normal child but above the average in intelligence. As the husband considered she had been the cause of the mother's death he did not want the infant, and she was offered to me for adoption. One of my native nurses adopted her by paying the sum of one yen. The child was still alive and well in November, 1940, when I left the district.

From the end of the patient's last menstrual period till the day of delivery was 320 days. It would be interesting to know just how long, under these circumstances, a child could live. It is evident that this one was near the end of active life, as when removed from the mother it did not at once show signs of life; but while I was still attending the mother the infant started to cry.

OTHER CASES

In 1914, in Tainan, Formosa, I had a case of full-term extra-uterine pregnancy in a woman aged 42. This case was reported in the *China Medical Journal*, 1915, 29, 14, from which I quote: "Child removed from its bed with as much of the surrounding sac as could safely be taken away, then the margins of the sac were stitched to the abdominal opening and the cavity packed with two towels. The bowel was adherent all around the sac. Patient ran a septic temperature from 97° to 103° F. for thirty-seven days, after which the temperature remained normal and she made an uninterrupted recovery. Seen five months after operation the wound had quite healed, and her only discomfort was pain on menstruating. . . . The child (dead) weighed 7 lb. and was well formed."

In 1934, in Taihoku, in one ward at the same time were two cases of extra-uterine gestation ruptured in the earlier months; and two full-term extra-uterine cases, ages 38 and 40, each with dead child. All four patients recovered. The treatment in each full-term case was the same: the placenta was undisturbed, cavity lightly packed, and neither gave any further anxiety—this in contrast to the method of immediate removal of the placenta, when "the immediate after-treatment of such cases is, always an anxious matter" (Whitehouse, 1935). One of these patients was running a septic temperature on admission, and her wound healed two or three weeks before the other non-febrile case. In none of these last three cases was there any haemorrhage in the sac or peritoneal cavity.

The point in treatment I wish to make is that by marsupialization and allowing the placenta to disintegrate and come away gradually, without over-zealous use of forceps and scissors, even with the risk of sepsis and secondary haemorrhage, the total risks involved are fewer than when an attempt is made to remove the placenta at once, which may be met by "formidable technical difficulty" and "haemorrhage of the most severe kind . . . very difficult to control" (Whitehouse, 1935).

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