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PNEUMONIA IN NEWBORN INFANTS

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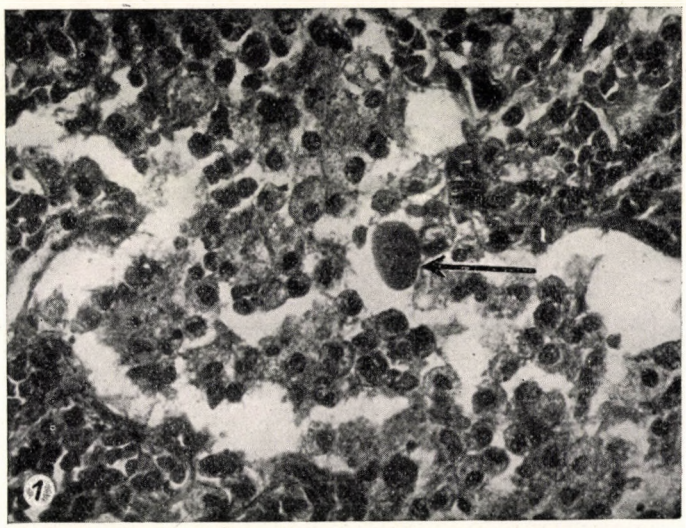
According to both earlier and recent examinations, pneumonia is a significant factor contributing to the mortality of the newborn. To clarify its aetiology is of great importance with respect to prevention and effective treatment alike. In the newborn, its diagnosis during life is often difficult or not possible at all and it is only by histological and bacteriological examination that it becomes possible to reveal the exact nature of the process.

In infants less than one week old aspiration plays an important rôle in the development of pneumonia which is often caused by aspiration of infected amniotic fluid, sometimes before birth (STAEMMLER), but mainly during delivery (CANON, GUILHEM and MAYER). After birth the newborn infant frequently aspirates milk or gastric contents (MORAN ; RHANEY and MACGREGOR). Infection, mostly bronchogenic, at other times haematogenous, is a most significant aetiologic factor (ROHMER et al.); haematogenous infection may seldom cause pneumonia *in utero* (THAISZ). The significance of pulmonary haemorrhages and oedema in the development of pneumonia in the newborn is well known (RIBADEAU—DUMAS and HÉRAUX) and recently the rôle of lesions of the central nervous system has also been stressed (SOFIYENKO).

Examinations

The lungs of 153 newborn infants (less than one week old) were examined microscopically. 54 of these infants had been stillborn and 99 had died within one week of birth. Their weight ranged from 600 g to 6000 g, on an average 2300 g. In 42 instances pneumonia has been revealed at the autopsy ; 80 per cent of those were aspiration bronchopneumonia. Aspiration is fairly frequent in newborn infants and we have observed it in 63 per cent of our 153 cases. In about one third of them, exactly in 32 per cent, pneumonia was caused by aspiration. The aspirated material consisted frequently of an amorphous material staining pink with eosin, rich in lipids and resembling fibrin, usually originating from the vernix caseosa. In some newborn infants milk had been aspirated. In these cases

the milk was found in the alveoli as a substance staining light-red with eosin, surrounded by mononuclear cells and neutrophile leukocytes, as well as by lipophages (fig. 1). A marked haemorrhagic inflammatory reaction, haemolysis and erythrocyte "shadows" around the aspirated material are indicative of vomitus containing gastric acid. The histological picture of aspiration bronchopneumonia



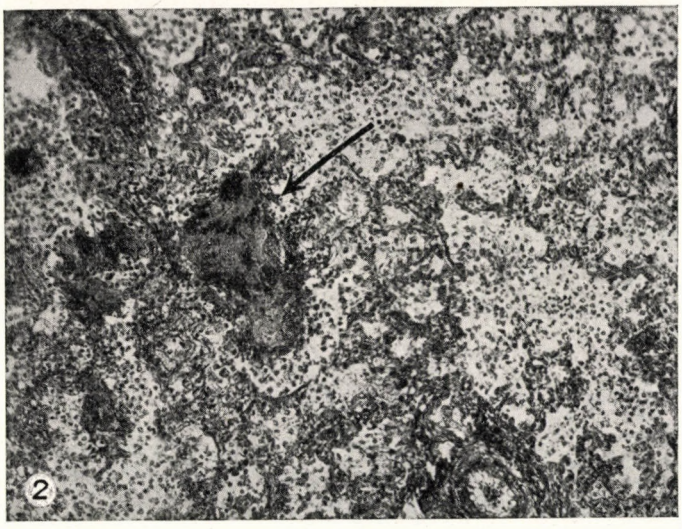


Fig. 1. Milk aspiration pneumonia. The rest of the aspirated milk stains a homogenous red with eosin (arrow); around it numerous desquamated alveolar epithelial cells containing fat droplets (lipophages) are seen. (Autopsy No. 422/1953. 4 days old infant. Haematoxylin-eosin stain. High magnification)

Fig. 2. Aspiration bronchopneumonia in 6 days old infant. The alveoli are filled with neutrophile leukocytes and some desquamated epithelial cells. The arrow indicates meconium in the alveoli. (Autopsy No. 56/1953. Farkas—Mallory stain)

resembles that of common bronchopneumonia and differs from the latter only in the aspirated material found beside the inflammation (fig. 2).

Pulmonary haemorrhage may also induce pneumonia in the newborn. Massive pulmonary haemorrhages in the lungs were observed in about 30 per cent of our cases ; in nine of these was pneumonia present. The haemorrhages were considered primary if beside the areas with haemorrhagic inflammation there were in the interstice and the alveolar lumina also areas of haemorrhage

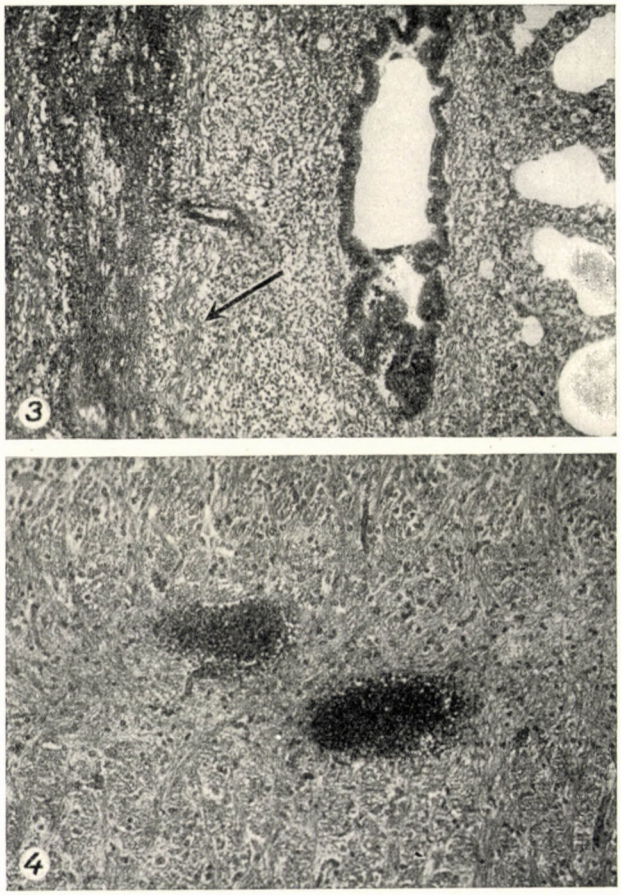
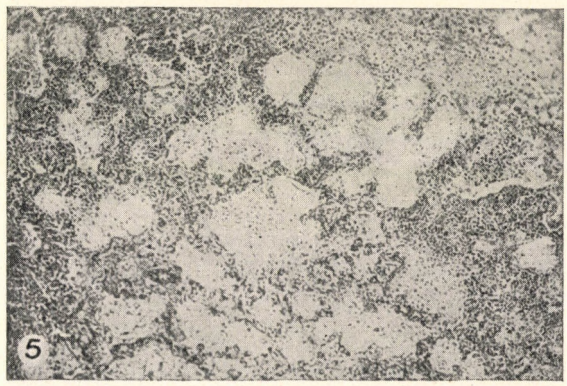


Fig. 3. Interstitial pneumonia in stillborn infant. In the longitudinal section of the vascular wall leukocytes and round cells are seen, which infiltrate also the bronchial wall. Thick interalveolar septa with marked cellular infiltration. (Autopsy No. 447/1952. Haematoxylin-eosin stain)
Fig. 4. Petechiae in the cerebral pons in one day old infant with pneumonia. (Autopsy No. 482/1953. Haematoxylin-eosin stain)

without any inflammation. In 47.6 per cent of the cases with pulmonary haemorrhage were there softening and haemorrhage in the central nervous system.

In some of the cases with pneumonia neither aspiration nor haemorrhages could be demonstrated. Their histological picture corresponded to that of common bronchopneumonia and they were usually due to aerogenic infection. In two cases the perivascular, subpleural localisation of the foci suggested a haemato-



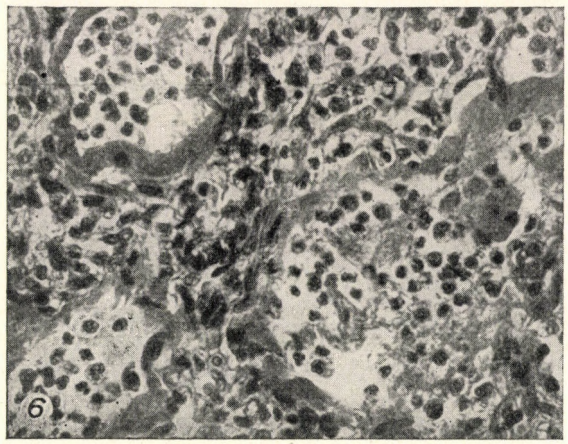


Fig. 5. Pulmonary gangrene induced by aspiration pneumonia. The necrosis of the lungs is well visible, the structure has become indistinct. Numerous fragmented pyknotic nuclei can also be observed. (Autopsy No. 417/1952. 5 days old infant. Haematoxylin-eosin stain)
Fig. 6. Alveolar walls lined with hyaline membrane ; in the lumina, neutrophile leukocytes and some desquamated alveolar epithelial cells. (Autopsy No. 485/1953. 2 days old infant. Haematoxylin-eosin stain)

genous origin from a purulent focus situated elsewhere in the organism.

In 8 stillborn infants and in 5 infants less than one day old was bronchopneumonia present, resembling at gross examination and also microscopically the features described above.

Interstitial pneumonia was observed in one stillborn infant. Infiltration with neutrophile leukocytes and mononuclear cells was most definite around the vessels from where it spread into the interstice. There was some aspirated amniotic fluid in the alveoli. The bronchi were intact, but in some areas inflammation had spread from the vessels onto the external layer of the bronchial walls (fig. 3). According to the histological picture, the case was one of haematogenous intrauterine interstitial pneumonia ; lesions indicative of syphilis have not been found.

Extensive lesions of the central nervous system (haemorrhages, softening of the brain), caused by birth injury have been found in 23 of the cases with pneumonia. Slight microscopic changes (petechiae, microscopical cerebral softenings, glia nodules) occurred in further 5 cases (fig. 4), their detailed description, however, is not within the scope of this paper.

Among the complications of pneumonia we have observed abscess and gangrene formation in four instances (fig. 5). In cases of extensive pneumonia alveolar emphysema was nearly always present and there was often interstitial emphysema, which, if extensive, spread also into the mediastinum. In 5 cases the alveolar walls were lined with a hyaline membrane (fig. 6).

Bacteriological examinations have been made in a few instances only. In these cases *Staphylococcus aureus*, *Streptococcus haemolyticus* or *Escherichia coli* were isolated from the lungs.

Discussion

As seen above among the pneumonias in newborn infants, those caused by aspiration of amniotic fluid were the most frequent. Infected amniotic fluid causes pneumonia, in some cases even gangrene. SCHULER and JAKAB have shown that amniotic fluid may produce pneumonia not only by infection, but also by its rich lipid content. The clinical significance of these lipid pneumonias consists in their weak response to therapy.

Pulmonary haemorrhage is fairly frequent in newborn infants. Smaller haemorrhages, occurring as a rule in the interstice or around the smaller blood vessels, are of no great importance. They are produced by asphyxia, less frequently they are part of haemorrhagic diathesis. Massive haemorrhages may break into the alveolar lumina and being good nutrient media for bacteria, develop frequently into pneumonia. Lesions of the central nervous system, *viz.* birth injuries may be often responsible for the development of massive pulmonary haemorrhage which rapidly may turn into pneumonia (SCHULER and JAKAB). This was well shown by one of our cases, where in the lungs of a full time infant, on a haemorrhagic basis severe bronchopneumonia developed. This was confluent over both sides and spread dramatically in about 20 hours almost over the whole lung and resulted in death (*Escherichia coli* and *Streptococcus haemolyticus* were isolated from the lungs).

This case confirms our observation that in newborn infants bronchopneumonia may take a few hours only to develop. We do not agree with the view held by many authors that all pneumonias in infants who died within 24 hours or even within three days after birth, are intrauterine pneumonias. Undoubtedly, the infection is often, but not exclusively caused by intrauterine aspiration, as proved by our case mentioned above. The development of pneumonia, even if induced by aspiration, occurs often in postnatal life ; it should be considered intrauterine only if pneumonia is demonstrable at birth already, or it is revealed in a stillborn infant.

Intrauterine pneumonia is nearly always induced by aspiration of amniotic fluid and is rarely haematogenous. Aspiration occurs in consequence of asphyxia before birth or during labour, or of lesions of the central nervous system ; these are frequent in prolonged or complicated delivery. In these cases pneumonia is present already at birth.

Although intrauterine pneumonia is usually bronchopneumonia, in one instance we found interstitial pneumonia in a stillborn infant. Plasmacellular interstitial pneumonia, a condition with characteristic clinical and pathological features, may appear in the newborn, although commonly it occurs in 2 to 3 months old prematurely born infants. In the newborn, interstitial (not plasmacellular) pneumonia appearing in epidemics or sporadically has been observed by ADAMS, who could demonstrate inclusion bodies in the lungs and therefore suggested viral origin. This latter type of pneumonia is different in aetiology, course and pathological pattern from interstitial plasmacellular pneumonia.

VISHNEVSKAYA, as well as SKHVORTSOV, believe that the majority of interstitial pneumonias in the neonatal period is spread from an inflammatory focus located elsewhere in the organism, e. g. in the umbilicus. Naturally, in addition to these forms produced by some unknown virus, known viruses (e. g. inclusion body disease, influenza) may also cause interstitial pneumonia.

In the literature we have found no mention of intrauterine interstitial pneumonia, although such pneumonia may occur. A case has been observed where the inflammation had spread from the vessels to the interstice ; the process was considered haematogenous. The infant's mother had been healthy during pregnancy, nevertheless we believe that some latent infection, bacteriaemia of the mother had passed through the placenta.

As seen, aspiration and pulmonary haemorrhages are important aetiological factors in the pneumonia in newborn infants. They occurred in 88 per cent of our cases. They were mostly consequential upon prolonged or complicated delivery, resulting in some lesion, most frequently in the central nervous system (brain, spinal cord and meninges). Occasionally the lesion of the peripheral nervous system may be considerable. In one of our cases where the vagus nerve in the thorax was surrounded by a massive haematoma, much aspirated material was found in the lungs. Prolonged or complicated birth and birth injury have

accounted for 47.6 per cent of the cases of pneumonia in our material. The importance of these factors is well reflected by the observation of CORNER, KISTNER and WALL that after prolonged labour the normal perinatal mortality rate of 3.7 per cent increased to 18.3 per cent. On the strength of these data the question arises whether in the presence of such injury it would not be advisable to administer antibiotics for some days after birth as a prophylactic means. This appears to be the more justified, since the clinical diagnosis of pneumonia is uncertain in the newborn. From among foreign investigators SOFIYENKO has come to similar conclusions. MUHL has achieved favourable results in such cases with the prophylactic administration of penicillin. NOVÁK succeeded in reducing by 50 per cent the incidence of perinatal pneumonias. From the discussion following our lecture at the Congress of Hungarian Paediatricians in 1953 we have understood that in this field encouraging results have been achieved also in Hungary. On the strength of our own examinations and the above data we believe that a study of this problem on extensive clinical material might lead to a decrease of the incidence of pneumonia and consequently to a decline of perinatal mortality.

Histological examination of the central nervous system has frequently shown, apart from birth injuries, other marked lesions (petechiae, softening of the brain). Some of these lesions have been described by SOFIYENKO, who considered them to be secondary changes.

The complications of aspiration pneumonia include often abscess and gangrene formation. The frequent occurrence of interstitial emphysema in infancy is accounted for by the low elasticity of the lungs.

The hyaline membrane occurring in the lungs of premature infants is a rather rare complication, which may be present independently of pneumonia. Reports in the literature indicate that it occurs in more than 40 per cent of the newborn infants (POTTER). We have observed it considerably less frequently, altogether in 5 cases. On the basis of the histological picture and of data in the literature we believe that the hyaline membrane arises in such a way that a fluid rich in proteins, aspirated or exuded into the alveoli, cannot be absorbed and owing to forced respiration, becomes plastered to the alveolar and bronchial walls, obstructing thereby the respiratory passages.

There is an extensive literature on the problem the detailed discussion of which would exceed the framework of this paper.

It must be noted that pneumonia in early infancy is often a secondary process. We have observed several cases where the haematogenous origin could be proved microscopically. In 5 infants pneumonia was associated with some other disease and its primary nature was questionable. However, on the basis of the findings the pneumonia was considered primary in most cases (88 per cent), although its primary or secondary nature cannot be always proved by pathological examination.

Summary

(i) The lungs of 153 infants less than one week old have been examined microscopically. Pneumonia has been found in 42 cases.

(ii) 88 per cent of the pneumonias have been induced by aspiration or haemorrhage.

(iii) Pneumonia can develop within a few hours, hence in infants who died within 24 hours of birth pneumonia cannot with certainty be considered as intrauterine. In 8 cases pneumonia has been observed in stillborn infants and newborn ones who died within 24 hours of birth.

(iv) A case of congenital interstitial pneumonia has been described ; it is thought to have been haematogenous.

(v) In 47,6 per cent of the pneumonias has prolonged or complicated parturition, birth injury been demonstrated.

(vi) The complications of pneumonia include abscess and gangrene formation, extensive emphysema (frequently interstitial) and the development of a hyaline membrane. In contrast with the reports in the literature, hyaline membranes have been found in a few cases only.

(vii) Pneumonia in newborn infants is considered to be primary.

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ДАННЫЕ К ВОПРОСУ О ПНЕВМОНИИ НОВОРОЖДЕННЫХ, ВОЗРАСТА НЕ ВЫШЕ ОДНОЙ НЕДЕЛИ

Д. ШУЛЕР и К. БАЛОГ

1. Проводилось микроскопическое исследование легких 153 новорожденных, возраста не выше 7 дней. В 42 случаях была обнаружена пневмония.

2. 88% случаев пневмонии были аспирационного или геморрагического происхождения.

3. Пневмония может развиться в течение нескольких часов, и следовательно пневмонию новорожденных, умерших в течение суток, нельзя с полной уверенностью рассматривать как внутриутробную пневмонию. У внутриутробных плодов или плодов, умерших в течение родов авторы обнаружили пневмонию в 8 случаях.

4. Авторы дают описание врожденной межуточной пневмонии, которая по их мнению гематогенного происхождения.

5. В большой части случаев пневмонии (47,6%) авторы могли выявить затянувшиеся или сложные роды, или родовую травму. Они считают обоснованным в таких случаях проводить исследование эффективности профилактической подачи антибиотиков на большом клиническом материале.

6. Осложнениями пневмонии являлись абсцессы или гангрены, распространенные (часто интерстициальные) эмфиземы, так же как и образование т. н. гиалиновидной мембраны. В противоположность литературным данным, авторы обнаружили гиалиновидную мембрану сравнительно редко.

7. Авторы считают пневмонию новорожденных, возраста не выше одной недели, в большинстве случаев первичной пневмонией.

ZUR FRAGE DER PNEUMONIE IN DER ERSTEN LEBENSWOCHE

D. SCHULER und K. BALOGH jun.

1. Es wurden die Lungen von 153 Neugeborenen mikroskopisch untersucht, wobei in 42 Fällen Pneumonie festgestellt wurde.

2. Bei 88% wurde die Pneumonie durch Aspiration oder Hämorrhagie verursacht.

3. Die Pneumonie kann sich binnen wenigen Stunden entwickeln, und somit kann sie bei innerhalb 24 Stunden gestorbenen Neugeborenen nicht mit Sicherheit als intrauterin betrachtet werden. Bei intrauterin oder während der Entbindung Gestorbenen wurde in 8 Fällen Pneumonie festgestellt.

4. Ein Fall von kongenitaler interstitieller Pneumonie wurde auch beobachtet, deren Herkunft als hämatogen betrachtet sein dürfte.

5. Bei einem grossen Teil der Pneumonien (47,6%) konnte verzögerte oder komplizierte Geburt, oder Geburtsrtauma nachgewiesen werden. Es wäre demzufolge angezeigt, die Wirkung von prophylaktisch verabreichten Antibiotika an grösserem klinischen Material zu untersuchen.

6. Als Komplikationen der Pneumonie waren Abszess- bzw. Gangränbildung, ausgedehntes (nicht selten interstitielles) Emphysem, und Entwicklung von hyaliner Membran beobachtet; letztere kam im Gegensatz zu den literarischen Angaben nur selten vor.

7. Die Verfasser sind der Meinung, dass Pneumonie in der ersten Lebenswoche meistens primär ist.

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