Pneumonia in Newborn Infants

By

B. Steiner, Gy. Putnoky, Klára Kovács and Gy. Földes

Paediatric Department (Head: Dr. B. Steiner), Central Laboratory (Head: Dr. Gy. Putnoky) and Pathological Department (Head: Dr. A. Vécsei) Postgraduate Medical School, Budapest

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Infection, usually manifesting itself with pneumonia, is a significant factor in neonatal mortality, with death occurring during the first 28 days of life. Some twenty years ago it was responsible for 13.7 per cent of the neonatal deaths [17] and its incidence is still high [20]; for instance, in a postmortem study of 352 newborns pneumonia was revealed in 155 cases [9].

Pneumonia in the newborn may develop before, during or after birth. Transfer of pathogens from mother to foetus is the cause of prenatal pneumonia. Premature escape of the amniotic fluid may give rise to ascending infections. If the newborn is infected during delivery, it is from the genitals [20] or the intestines [1] of the usually healthy mother that the pathogens gain, mostly by aspiration, access to the infant's lungs, since prolonged labour and a premature rupture of the membranes promote the development of ascending infections. Adults, other infants and contaminated objects in the surroundings of the infant are the sources of postnatal infection.

Infections *in utero* are usually considered more dangerous than those acquired by inhalation because in the former case bacterially contaminated fluid gains access to the lungs [11]. Potter [23] attributes to aspiration the pneumonias developing the first postnatal days. According to Claireaux [6] about 50 per cent of the pneumonias arise in consequence of aspiration before and during delivery. The autopsy findings of 55 newborns [1] revealed massive aspiration in 17, moderate aspiration in 20, slight aspiration in 18 cases. The fact that very few bacteria were found in the pneumonic areas made it probable that the pathogenicity of bacteria was enhanced by congestion in the respiratory passages obstructed by the aspirated amniotic fluid, vaginal secretion or meconium. On the other hand, it was only in two instances that Penner and McInnis [22] could find a considerable amount of amniotic fluid in the lungs, while Torrey and Reese [36] isolated staphylococci from 50 per cent of 2-day-old and 90 per cent of 4 to 10-day-old infants, a sign of environmental infection.

The high incidence of infections acquired *in utero* or during delivery must be regarded as a warning that adequate preventive measures should

be taken before birth in certain instances and during labour in others. Such measures require a close co-operation between obstetrician and paediatrician; the prolongation of labour may be harmless for the mother when ascending infection has already induced pneumonia in the infant.

To institute adequate measures, two fundamental questions have to be cleared, *viz.* (i) which are the pathogens involved, and (ii) is there a difference between the pneumonia of the newborn and that of other patients in the paediatric age group.

Material

The correct diagnosis of neonatal pneumonia often presents difficulties [35]. It is easily confounded with the hyaline membrane syndrome, atelectasis, respiratory disturbances due to pulmonary and cerebral haemorrhage or malformations. Not even gross post-mortem examination always discloses it reliably. In the following, therefore, only histologically verified cases of pneumonia will be presented. There were 23 such cases in our material. Our investigations were extended in addition to 11 cases of hyaline membrane syndrome and 7 cases of atelectasis, all of them confirmed histologically. The post-mortem findings in 88 other newborns and 13 infants and young children were also considered.

Pathogenicity of the Isolated Bacteria

A problem we were repeatedly confronted with in earlier investigations [31—35] was the causal connection between the histologically verified pneumonia and the bacteria isolated from the coughed-up secretion or that obtained from the glottis, subglottis, bronchi, and needle biopsy material. First it was thought that the identity of bacteria recovered during life from the pharynx and those found in pure culture in the autopsied lung might be accepted as proof of a causal connection. Further considerations and some recent reports, however, have warned from drawing such definite conclusions. Provided the defence mechanism of the organism is unimpaired, there are no bacteria to be found in the lungs of healthy persons, while after death the lungs often contain bacteria with or without concomitant pneumonia.

The presence of bacteria in the lungs at autopsy may indicate several possibilities.

(1) The pneumonia had been due to the bacteria recovered post-mortem. This may be proved sometimes by a characteristic histology, and the identity of the micro-organisms isolated from the area of inflammation and the macrophages, and those cultured from the circulating blood during life. A characteristic feature in such cases is a mass of bacteria forming clouds not only in the smears but also in the histological sections of the focus [12].

(2) The pneumonia had not been caused by the isolated bacteria; these had gained access to the lungs secondarily as pathogens or saprophytes. For example, in cases of pneumococcal pneumonia the place of the *Diplococcus pneumoniae* destroyed by penicillin may be taken by *Ps. aeruginosa*. The situation is similar in cases of influenza pneumonia when staphylo-

cocci may act as secondary pathogens.

(3) The bacteria isolated post-mortem had gained their way into the lungs during agony. There are no signs of pneumonia, and the isolated bacteria are not pathogenic.

(4) The isolated bacteria had invaded the lungs after death. In this case it is not possible to infer the agent which had been responsible for the pneumonia.

We are ready to accept the criteria enumerated under (1), as sufficiently proving that pneumonia had been due to the bacteria recovered post-mortem from the lungs. In neonatal pneumonia, however, histologic changes characteristic of the pathogen and an abundant bacterial flora are infrequent. It was, therefore, endeavoured to ascertain in addition (i) the frequency of bacterial invasion of the lungs from the upper respiratory tract, and (ii) the diagnostic value of the identity of postmortal pure cultures from the lungs with the bacteria isolated from the throat secretions during life.

KNEELAND and PRICE [15] could isolate staphylococci from 50 per cent of the cases in which autopsy revealed pneumonia and from 30 per cent of those in which there was no sign of pneumonia. Inference as to the causative role of the isolated bacteria seemed to be more reliable if only pure cultures were taken into account. While pure cultures of staphylococci were obtained in 10 cases of pneumonia, it was only in a single case that a pure culture occurred without pneumonia. The corresponding figures were six and zero in respect of *Ps. aeruginosa*, and two and zero in that of *Proteus vulgaris*.

Still, no general conclusions could be drawn from these data because pure cultures of *Klebsiella — Aerogenes* strains could not be obtained in any of the pneumonia cases, but were isolated from four cases without pneumonia. Similarly, *E. coli* was isolated only from one case with pneumonia, while from four without pneumonia.

KNEELAND and PRICE found that a given bacterium grown in pure culture from adult autopsy material was not a reliable indication of the pneumonia having been caused by that same microorganism.

It is, as has been noted, necessary that bacteria should be demonstrated in the area of pneumonia by means of culturing and staining before being accepted as the true causative agent [1, 12, 22].

As regards the interrelation between pulmonary infection and the length of agony, KNEELAND and PRICE [15] found that after protracted agony (malignant tumours, renal disease, cardiac failure) the lung was seldom free from bacteria, while it was sterile in 63 and 73 per cent of the cases of rapid death from cerebral and coronary disease, respectively. In our present material a long agony was quite exceptional.

In addition to the above data which all refer to adults, our post-mortem studies of the lungs of 130 infants and young children yielded a positive bacteriological finding in 71 cases (55 per

cent). Among 88 newborns there were 17 in whom bacteria could be isolated neither from the throat before death, from the secretion aspirated from the lungs immediately after death, nor from the necropsied lungs. While 20 out of 102 throat secretions examined during life proved sterile, 59 proved sterile among 130 samples of pulmonary secretion obtained after death.

In our post-mortem material close to 50 per cent of the lungs were free from bacteria. On the evidence of 400 post-mortem examinations made within 36 hours after death, no bacterial invasion of the lungs occurs if the corpse has been kept in the refrigerator [24]. The pharyngeal flora does not reach the lungs within 36 hours following death except in cases of deep coma [27, 5]. This means that bacteria isolated in pure culture from autopsy material should not be disregarded, but their pathogenic significance cannot be accepted without further proof.

The bacterial flora in the 23 newborns with histologically verified bronchopneumonia was as follows.

E. coli, pure culture, ...	11 cases
E. coli and paracolon bacilli,	1 case
E. coli and Gram-positive cocci, ...	1 case
E. coli, *Staphylococcus* and Gram-positive cocci	1 case
E. coli and *Proteus*	1 case
Paracolon bacilli	1 case
Staphylococcus	1 case
Proteus and Gram-positive cocci	1 case
Gram-negative bacteria ..	1 case
No bacteria	4 cases

The bacterial flora in the 7 newborns with atelectasis consisted of Gram-positive cocci and diplococci in one case. This patient lived 48 hours. In the other 6 cases no organism could be cultured from the lungs.

The bacterial flora in the 11 newborns with histologically verified hyaline membrane was as follows.

Sterile	7 cases
E. coli and Gram-positive cocci	1 case
E. coli in one lung	1 case
Paracolon bacilli.....	1 case
Staphylococcus	1 case

It is seen that the microorganisms isolated in our material were conspicuously different from the usual pathogens of pneumonia in adults and in children of the higher age groups. While potential pathogens, such as *Diplococcus pneumoniae*, *Haemophilus influenzae*, *Streptococcus beta haemolyticus* were absent, and *Staphylococcus* rare, bacteria generally regarded as saprophytes occurred. Two of the four negative cases had been treated with antibiotics.

The views as to the pathogenicity of the bacteria found by us are contradictory. In the 1950 edition of NELSON's textbook no mention was made of *E. coli* as a causative agent of newborn pneumonia. In FANCONI and WALLGREN's textbook [8] *E. coli* is said to be a potential pathogen only during the first week of life. In 1957, SMITH [29] already ascribed the respiratory diseases of newborns to coli-

form organisms, Gram-negative bacteria or penicillin-resistant staphylococci. *Nelson* [20] in 1960 already stressed the significance of *E. coli* and regards it as the second most frequent cause of neonatal infections, while we ourselves consider *E. coli* to be the commonest aetiologic agent of neonatal pneumonia. KNEELAND and PRICE found also *Ps. aeruginosa* and *Proteus* in several cases.

BERNSTEIN and WANG [1] examined 55 cases of neonatal pneumonia, and their results furnish useful data in respect of the pathogenic significance of the bacteria found in our material. It was in 34 cases that they could demonstrate the pathogen both by culturing and histologically, while in further 12 cases they found bacteria in the macrophages or in the immediate vicinity of the amniotic debris. These 46 cases were accepted by them as positive. They qualified as doubtful 6 cases in which cultivation did and histology did not give positive results. No bacteria were discovered in 3 cases. The organisms demonstrated by culturing as well as histologically were *E. coli* in 9 cases; paracolon bacilli in 5 cases; *A. aerogenes* in 3 cases; *Kl. pneumoniae* in 2 cases; *Ps. aeruginosa* in 4 cases; *Streptococcus* in 4 cases (of which *Str. alpha-haemolyticus*, 1 case; *Str. beta-haemolyticus*, 2 cases; *Str. non-haemolyticus*, 1 case); *Staphylococcus aureus* in 4 cases; and *Staphylococcus albus* in 3 cases. (The two strains of *Str. beta-haemolyticus* may have belonged to groups C or D, present in the intestinal tract under physiological conditions.) Bacteria revealed by histology but not isolated by culturing were mostly Gram-negative. The incidence of staphylococci was less in our material. This must have been due to the fact that in our Institute the rate of staphylococcus carriers is unusually low [34].

The second problem to be decided was whether just a single kind or several organisms were responsible for the pneumonia. Our 23 cases yielded in three instances two, in one instance three, different kinds of bacteria. BERNSTEIN and WANG [1] demonstrated histologically several types of organisms; staphylococci with Gram-negative bacteria, and Gram-negative cocci with coliform bacteria. The combination of streptococci (viridans and non-haemolytic) and coliform bacteria has been mentioned also by MCGREGOR [17]. The infrequent occurrence of a mixed bacterial flora would be surprising were most of the neonatal pneumonias due to aspiration.

DISCUSSION

According to the report of SHIFLEY et al. [26], in 1926 the most common aetiological agents of pneumonia were *H. influenzae*, *Streptococcus haemolyticus* and *Staphylococcus haemolyticus aureus*. Earlier *Diplococcus pneumoniae* had been regarded as the most frequent cause of pneumonia. By now, *Diplococcus pneumoniae* has lost much of its importance, while Gram-negative bacteria *(E. coli, A. aeruginosa, Proteus)* became frequent pathogens [13, 14].

Certain forms of staphylococci are also claiming an increasing number of victims. The data of KNEELAND and PRICE [15] are instructive: while in the earlier material of their institute *Diplococcus pneumoniae*, *H. influenzae* and *Str. beta-haemolyticus* had been responsible for the cases of terminal pneumonia, in 1960 the aetiologic agents were *Staphylococcus* [17 cases), *Ps. aeruginosa* (2 cases), *Proteus* (1 case), *E. coli* (1 case), *Klebsiella-Aerogenes* (2 cases) and higher bacteria (3 cases). They attribute the recent predominance of these organisms to the widespread use of antibiotics.

The bacterial flora seen in neonatal pneumonia shows much similarity to that observed in the pneumonia of aged patients. This phenomenon cannot be ascribed to the influence of antibiotics since most of the newborns examined by BERNSTEIN and WANG received no, or hardly any, antibiotic treatment. The predominant *E. coli* presumably originates from the maternal genitals, while the staphylococci must come from the environment.

The observation that newborns and aged persons are especially sensitive, and healthy adults generally more resistant, to coliform bacteria makes it probable that the immune mechanism in respect of these pathogens is not yet operative in the newborn and no longer operative in aged individuals. This possibility seems to be substantiated by the fact that BERNSTEIN and WANG [1] found an abundant bacterial flora in not more than 6 cases of acute diffuse pneumonia out of a total of 49; this shows that a small number of bacteria sufficed to induce foetal disease in these cases.

It is interesting to note the phenomenon not sufficiently emphasized in the literature that newborn infants are rarely infected by the usual pathogens. The explanation that the transfer of antibodies from mother to child is limited cannot be accepted. The transfer of antibodies against *H. influenzae* is practically nil, and it is nevertheless very rare that a newborn baby should fall victim to the disease. It has been pointed out by RAUSS [25] that, notwithstanding the regularly observable presence of staphylococcus antitoxin in the umbilical blood, infants display a striking susceptibility to staphylococcal infections. NELSON [20] remarks that, so far, no satisfactory explanation has been advanced in this respect.

The question arises whether intrauterine infections are not being overrated and environmental ones underestimated. PENNER and MCINNIS [22] hold that most determinations concerning the origin of bacteria recovered from the lungs are unreliable. KUTHY and LUSZTIG [16] as also OSBORNE [21] reject the supposition that pneumonia during the first three postnatal days is invariably of intrauterine origin, and recognize its validity only for the first day of life. Friedländer's bacillus may be present in the mouth and the upper respiratory passages of 1 to 5 per cent of normal individuals [3] so that it can pass over to the newborn. The youngest infant to contract staphylococcal pneumonia in the mate-

rial of BLOOMER et al. [2] was 10 days of age. Bacteriological tests of pharyngeal secretions sampled during the first day of life rarely yielded positive results in our material, although if the infants had aspirated the contagious matter they would probably have swallowed it as well. SMITH [29] thinks that with an aseptic delivery the mouth and the pharynx of normal newborns is sterile at birth and its initial bacterial flora is always of environmental origin. Bacteria gain access to the upper respiratory tract of the baby from the mother's vagina if the obstetrical conditions are not quite up to the mark. SMITH mentions staphylococci, streptococci, diphteroid bacteria and a variable number of coliform bacilli as composing the bacterial flora in such cases. His data seem to be confirmed by the observation that the lochia contains few bacteria during the first 24 hours [10], while the vagina contains streptococci and staphylococci in 15 to 70 per cent of the cases [10]. It is worthy of note that, according to the findings of MONTES-GALLO [18] and in agreement with our own observations, no bacteria are present in the stomach of newborn infants during the first day of their life.

A survey of the data supplied by DUNHAN [7] and SMITH et al. [30] shows that, while 38 per cent of neonatal septicaemia were due to streptococci in 1933, these pathogens ceased to figure in the statistics of 1956. The percentage of *E. coli* rose from 25 to 66, that of *Ps. aeruginosa* from 2.5 to 13. The frequency of staphylococci fell from 28 to 20 per cent — a phenomenon that was probably due to local conditions. The other data supplied by FLESCH [4] concerning conditions in Hungary in 1912 are highly instructive in this respect: he mentioned streptococci, staphylococci and diplococci as the principal agents of neonatal septicaemia — all of them organisms which have been practically absent in our recent cases of infantile pneumonia.

Although additional data have to be collected before definite conclusions can be drawn, certain facts can nevertheless be stated even at the present stage. Coliform bacilli were the principal agents recovered post-mortem from our material of neonatal pneumonia. While it was not possible to prove that the pneumonia had actually been caused by these organisms, it is safe to regard them as potential pathogens since no other bacteria were found. The presence of bacteria in the lungs is by no means a physiological phenomenon; 45 per cent of our material had no bacteria in the lungs. BERNSTEIN and WANG [1] are definitely of the view that the observed coliform bacilli did not enter the lungs either during agony or after death but were true pathogens. It follows that the possibility of postnatal infections must be taken into account more carefully than at present, and this the more so as the considerable change in the aetiological agents of neonatal disease during the last decade shows a perfect parallelism with the change in aetiological agents of neonatal pneumonia.

Therapeutical Conclusions

Since most textbooks disregard the fact that the causative agents of pneumonia are different in the newborn and at later ages, they recommend the administration of penicillin and streptomycin in the usual dosage. Nelson [20] in 1960 already recommended the application of antibiotics which antagonize *E. coli* and other Gram-negative bacteria as the most common invaders of the neonatal organism. The usual doses of penicillin are inefficient against these pathogens and the value of streptomycin is always uncertain so that broad-spectrum antibiotics seem to be the drugs of choice. Of these, chloramphenicol has been found to give rise to unpleasant side effects, especially in prematures [37], although in our material there was only one such case. To avoid untoward effects, tetracycline preparations should be used while erythromycin and the recent potent penicillin preparations should always be kept at hand. We are not opposed to the combined use of antibiotics. Data are being collected at present with a view to ascertaining whether treatment started before and during delivery is really quite as favourable for the newborn as it ought to be according to theoretical considerations.

Summary

Bacteriological examination of the secretions during life and after death has been made in 23 newborns with pneumonia, 11 with hyaline membrane and 7 with atelectasis. Coliform bacteria have been isolated from the lungs of 17 infants with histologically verified neonatal pneumonia. As no other organisms were isolated they were regarded as potential pathogens. No organisms could be isolated from 6 cases of atelectasis.

Pure bacterial cultures obtained from the lungs after death and fatal pneumonia need not be connected causally. The pathogenicity of the isolated organisms may be taken for granted only if they are identified both by culturing and histologically.

Post-mortem tests revealed a sterile lung in 45 per cent of our 130 cases of infantile pneumonia.

As a treatment, tetracycline, erythromycin and potent recent penicillin preparations are recommended. A combination of antibiotics may be indicated in certain cases. The recent predominance of coliform organisms in neonatal pneumonia seems to call for treatment before and during delivery in certain cases.

References

1. Bernstein, I., Wang, J.: Pathology of Neonatal Pneumonia. Amer. J. Dis. Child. **101,** 350 (1961).
2. Bloomer, W. E., Giamonda, S., Lindskag, G. E., Cooke, R. E.: Staphylococcal Pneumonia and Empyema in Infancy. J. thorac. Surg. **30,** 25 (1955).
3. Bloomfield, A. Z.: The Mechanism of the Bacillus Carrier State with Special Reference to the Friedländer Bacillus. Amer. Rev. Tuberc. **4,** 841 (1921).
4. Bókay, J., Flesch, A., Bókay, Z.: A gyermekorvoslás tankönyve. Mai, Budapest (1912).
5. Burro, C.: Postmortem Bacteriology. J. inf. Dis. **54,** 395 (1936).
6. Claireaux, A. E.: Neonatal Pathology, in Modern Trends in Pediatrics ed. A. Holzeland, J. P. M. Tizard, New York (1958).
7. Dunhan, E. L.: Septicaemia in the Newborn. Amer. J. Dis. Child. **45,** 229 (1933).
8. Fanconi, G., Wallgren, A. ed., Lehrbuch der Pädiatrie, 4. Aufl. Schwabe, Basel (1956).
9. Gábor, P., Bartók, I.: Intrauterine Pneumonie als Todesursache beim Fetus. Zbl. allg. Path. path. Anat. **95,** 217 (1956).
10. Greenhill, J. P., Delee, J. P.: Principles and Practice of Obstetrics. 10th Ed. Saunders, Philadelphia (1951).
11. Hamburger, M., Robertson, O. H.: Studies on the Pathogenesis of Experimental Pneumococcus Pneumonia in the Dog. J. exp. Med. **72,** 261 (1940).
12. Haranghy, L.: Részletes Kórbonctan. Medicina, Budapest (1960).
13. Jeney, E.: Az antibioticum resistentia elméleti kérdései MTA. Biol. Orvostud. Oszt. Közl. (Budapest) **11,** 239 (1961).
14. Kikuth, W.: Der moderne Hospitalismus aus mikrobiologischer und hygienischer Sicht. Dtsch. med. Wschr. **85,** 1920 (1960).
15. Kneeland, Y., Prince, K. M.: Antibiotics and Terminal Pneumonia. A Postmortem Study. Amer. J. Med. **29,** 967 (1960).
16. Kuthy, I., Lusztig, G.: A magzatok intrauterin pneumoniája. Magy. Nőorv. Lapja. **21,** 42 (1960).
17. McGregor, A. R.: Pneumonia in the Newborn. Arch. Dis. Childhood. **14,** 323 (1939).
18. Montes—Gallo, D., Saari, R.: The Acidity and Bacterial Content of the Gastric Juice. Ann. paediat. Fenn. **6,** 185 (1960).
19. Nelson, W. E., ed. Textbook of Pediatrics, 7th ed. Saunders, Philadelphia (1959).
20. Nelson, W. E.: On the Role of Infections in Neonatal Mortality. J. Pediat. **56, 257** (1960).
21. Osborne, G. R.: Congenital Pneumonia. Lancet **1,** 511 (1954).
22. Penner, D. W., McInnis, A. G.: Intrauterine and Neonatal Pneumonia. Amer. J. Obstet. Gynec. **69,** 147 (1955).
23. Potter, E. L.: Pathology of the Fetus and the Newborn. Yearbook Publishers, Chicago (1952).
24. Putnoky, Gy.: Results of Bacteriological Studies of 400 Necropsies. Amer. J. clin. Path. **7,** 275 (1936).
25. Rauss, K.: A staphylococcus fertőzések mikrobiologiai és járványtani vonatkozásai. Orv. Hetil. (Budapest) **100,** 1806 (1960).
26. Shifley, G. I., Hanger, F. M., Dochez, A. P., Mills, K.: Bacterial Flora of Nose and Thorax in Health and Upper Respiratory Infection. Proc. Soc. exper. Biol. (N. Y.) **23,** 258 (1926).
27. Smillie, W. G., Duerschner, D. R.: The Epidemiology of Terminal Bronchopneumonia. Amer. J. Hyg. **45,** 1 (1947).
28. Smith, J. A. M., Jeninson, R. F., Langley, F. A.: Perinatal Infection and Perinatal Death. Clinical Aspects. Lancet **2,** 903 (1956).
29. Smith, M. H. D.: Bacterial Pathogens of the Respiratory Tract of the Newborn Infant. Pediatric Clinics of North America. Saunders, Philadelphia (1957).
30. Smith, R. T., Platon, E. I., Good, R. A.: Septicemia of the Newborn. Current Status of the Problem. Pediatrics **17,** 549 (1956).
31. Steiner, B., Putnoky, Gy.: Klebsiella pneumonia halmozott előfordulása koraszülött és csecsemő osztályon. Orv. Hetil. (Budapest) **97,** 323 (1956).
32. Steiner, B., Putnoky, Gy., Kovács K., Szabon, J.: Aimed Antibiotics Treatment of Pneumonia on the Basis of Tests Carried Out with Subglottic Swabs. Acta paediat. (Upsala) **47,** 172 (1958).
33. Steiner, B., Putnoky, Gy., Kovács, K., Szabon, J.: A pharinx, glottis és subglottis bakterium flórájának vizsgálata gyermekben. Theoretikus és gyakorlati megfigyelések. Orv. Hetil. (Budapest) **101,** 1130 (1960).

34. Steiner, B., Putnoky, Gy., Holló, T.: A resistens staphylococcus aureus haemolyticus jelentősége intézetünk újszülött és csecsemőosztályán. Orv. Hetil. (Budapest) **102,** 116 (1961).
35. Steiner, B., Putnoky, Gy., Kovács, K., Szabon, J., Földes, Gy.: Az újszülöttek és csecsemők légzőtractusának bakteriologiai vizsgálata tüdőgyulladásban. Orv. Hetil. (Budapest) **102,** 244 (1961).
36. Torrey, I. C., Reese, M. K.: Initial Aerobic Flora of Newborn Infants. Amer. J. Dis. Child. **69,** 208 (1949).
37. Weiss, Ch. F., Gluko, A. I., Weston, J. K.: Chloramphenicol in Newborn Infants. Physiologic Explanation of its Toxicity when Given in Excessive Doses. New Engl. J. Med. **262,** 181 (1960).

Dr. B. Steiner
Szabolcs u. 33
Budapest XIII., Hungary