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Published in:
Acta Obstetricia et Gynecologica Scandinavica

DOI:
10.1034/j.1600-0412.2001.d01-151.x

2001

Acta Obstet Gynecol Scand 2001; 80: 511–518
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Acta Obstetricia et Gynecologica Scandinavica
ISSN 0001-6349

ORIGINAL ARTICLE

Intrauterine infection may be a major cause of stillbirth in Sweden

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Acta Obstet Gynecol Scand 2001; 80: 511–518. © Acta Obstet Gynecol Scand 2001

Aim of the study. To investigate intrauterine infection as a cause for unexplained stillbirth.
Methods. Chorioamnionitis was studied in a material of stillbirths (117 subjects from the years 1985–1994) from a region in the south Sweden. Control material (126 alive and healthy newborns and with healthy mothers) was gathered from the same region.
Results. Chorioamnionitis was a common diagnosis both with stillbirths and 'healthy' deliveries (82 and 68%, respectively). Extension of the inflammation to decidua basalis was seven times more common among stillbirths than among controls (odds ratio 7.2, confidence interval 2.8–21.9). The most common bacteria found at cultures were *Escherichia coli*, Coagulase negative staphylococcus, *Enterococcus faecalis* and group B Streptococcus. The risk for stillbirth was doubled if both inflammation and bacteria were present (odds ratio 2.3, confidence interval 0.92–5.8). Meconium discharge was more common among stillbirths than controls (odds ratio=4.7, confidence interval 1.7–14). There were no differences in any respect regarding macerated and non-macerated stillbirths. Our findings are similar to the results from studies in developing countries except for the higher incidence of stillbirths in such countries.
Conclusions. Thus, a large part of otherwise unexplained stillbirths might be due to ascending infections.

Key words: chorioamnionitis; stillbirth

Submitted 31 May, 2000
Accepted 15 January, 2001

In Sweden a stillbirth is defined as a fetus, who died *in utero* and is delivered after 28 completed gestational weeks. Known conditions causing stillbirth are placental insufficiency due to eclampsia or lupus anticoagulant syndrome in the mother, maternal diabetes mellitus, complex malformations, chromosomal anomalies, certain infections e.g. group B streptococci (GBS), *Listeria* and different viruses. However, in many stillbirths the cause remains unknown.

Abbreviations:
GBS: group B streptococci; OR: odds ratio; PMNs: polymorphonuclear leucocytes; CI: confidence intervals; TSB: tryptic soy broth.

Chorioamnionitis was reported to be the cause of death in 7.9% of stillbirths in East Lausing, Michigan, USA (1) and in 2% in Helsinki, Finland (2). In Toronto, Canada, Quinn et al. (3) found 71% of chorioamnionitis among stillbirths with no other cause of death versus 22% among stillbirths with other proven causes of death.

The placenta and fetus can be infected by two major pathways: the hematogenous (transplacental) route and the ascending, amniotic (transcervical) route. Hematogenous infection produces an inflammatory response in the villi (villitis) with dominating lymphocytic infiltration. The etiologic agents are viruses, certain bacterial species (spirochetes, *Listeria*) and protozoa (*Toxoplasma gon-*

dii). In ascending intrauterine infection (chorioamnionitis) bacteria from vagina spread through the uterine cervix between the chorion and amnion into the amniotic fluid, to the chorionic and/or to the basal plate of the placenta. Intrauterine infection is a unique situation, in which two individuals are exposed to infection at the same time. Morphologically, maternal as well as fetal responses may occur. Polymorphonuclear leucocytes (PMNs) in the free membranes, subchorionic fibrin, chorionic plate of the placenta and decidua basalis are maternal, while PMNs in the walls of arteries and veins inside the chorionic plate and the umbilical cord are of fetal origin.

More than 130 different bacterial species may be involved in intrauterine infections (4). Several studies have shown a relationship between bacterial isolation from free membranes (5), amniotic fluid (6) as well as placental villous tissue (3) and chorioamnionitis, preterm labor (5), perinatal morbidity and mortality (3). GBS, *Fusobacteria, Escherichia coli* (*E. coli*), *Bacteroides* and *Ureaplasma* usually cause inflammatory response in the membranes (5). Intrauterine bacterial invasion may occur without inflammatory response in the fetus or the placenta. In some cases of chorioamnionitis with PMNs infiltration no growth of bacteria is found. But mostly an inflammatory lesion in the chorioamniotic membranes seems to serve as a marker of microbial invasion (6). It was shown in experiments with rabbits that inoculation of *E. coli* induced inflammatory response in the endometrium, amnion and chorion (7), and positive cultures from the same localizations as well as pregnancy losses (7, 8). However, similar injections of sterile exogenous irritants such as meconium, gastric juice, acid, India ink, did not result in chorioamnionitis (9).

Intrauterine infection is regarded as an important cause of stillbirth in developing countries (4, 10, 11). The prevalence of acute chorioamnionitis tends to be higher in developing than in industrial countries (10). Salafia et al. (12) found a prevalence of 4% of acute chorioamnionitis in uncomplicated term pregnancies in Connecticut, USA and Payne et al. (13) reported a prevalence of 24% of chorioamnionitis in a British population. However, the intrauterine infection as a cause of stillbirth in well nourished communities has been questioned (14). The purpose of this study was to explore the incidence of intrauterine infection in stillbirths in a Swedish population.

Material and methods

The study is based on 117 stillbirths (gestational age 28 weeks to term), who were autopsied in the Department of Pathology of the University Hospital, Lund, Sweden. The study period was from August 1st 1985 to December 31st 1994. The material consisted of stillbirths due to placental insufficiency, known infections and due to unknown cause. Cases with multiple congenital malformations were excluded as well as cases in which bacteriological examination had not been performed because of lack of personal resources to perform the sterile procedures. No twins appeared in the material. At autopsy, material for bacteriological and morphological examination was taken from placenta and organs. All autopsies were performed by one pathologist (IH). All placental slides of stillbirths were reevaluated by another pathologist (ET) who also examined all the placentas from the controls. As controls we collected 126 placentas from normal singleton term deliveries from the Department of Obstetrics of the University Hospital, Lund, Sweden, between September 28th 1995 and November 17th 1995. The delivery was considered normal when a mother after vaginal delivery without complications went home with a healthy child. The macroscopical examination of the placentas was performed by three of the physicians (IH, EM, ET), and most specimens for histology and bacteriology were sampled by a pathologist (ET).

Culture sampling

Cultures were sampled from all the placentas and the external ears of the neonates and stillbirths. In stillbirths samples were taken from the throat, lung, heart blood, liver, brain and liquor. Stillbirths and placentas were put in sterile towels in the delivery room and brought to the pathology laboratory. The autopsy was performed within 24 hours after delivery. Placentas for control material were examined daily in the obstetric department. After the delivery, placentas as well as ear cultures were placed in the refrigerator (+4 °C). All cultures were grown within 24 hours of the delivery. The culture samples from placenta and organs were obtained by disinfecting with 70% ethanol, incising through the skin or chorionic plate with the sterile scalpel blade and taking a piece of tissue with new sterile pincers and scalpels. The samples from placental tissue were taken with care to avoid contact with the decidua basalis. The heart blood was taken from the right ventricle and liquor was taken suboccipitally with sterile syringes. For sampling of brain tissue the large fontanelle was opened and tissue samples were taken with new sterile tools. Ear and throat cultures were placed in Stuart's transport medium. Liquor and blood were put in sterile tubes. Tissue samples of placenta and or-

gans were put into sterile boxes for subsequent bacterial culturing.

Culture conditions

Samples taken from the external ears and throats as well as from liquor and heart blood were inoculated on blood agar (5% horse erythrocytes) and hematin agar. Heart blood and liquor were also incubated in Tryptic soy broth (TSB) and incubated at 37°C for two days and then subcultured on the same media. Hematin agar and one blood agar plate were incubated in 5% CO_2 atmosphere, and one blood agar plate was incubated anaerobically for two days. Tissue samples from placenta, lung, liver and brain were homogenized before being inoculated in TSB for two days, after which they were subcultured as above. Isolated microorganisms were typed to the species level according to the ASM Manual (15).

Chemicals

Agar base was purchased from LabM, Salford, UK, and TSB from Difco Laboratories, Detroit, Michigan.

Morphologic examination

Full autopsy with macroscopic examination of all the organ systems was performed. Maceration and meconium staining were noted. Samples from most organs for microscopical examination were taken. Five samples were taken from each placenta: umbilical cord next to placenta, a sample from the middle of the umbilical cord, a roll of the free membranes was performed from the border of rupture to the border of the placenta and two samples from each placenta, both including chorionic plate and decidua basalis. The tissue was fixed in 4% formaldehyde, and embedded in paraffin. Sections were performed and stained with hematoxylin and eosin. The degree of inflammation in the tissues was estimated as follows:

Grade 0=<5 PMNs/high power field
Grade 1=5–19 PMNs/high power field
Grade 2=20–49 PMNs/high power field
Grade 3=>50 PMNs/high power field
(high power field=ocular 10, objective 40)

The grade of chorioamnionitis was regarded as the most severe one in any of the localizations.

Statistical analysis

The study was analyzed as a case-control study, regarding the stillbirths (n=117) as cases and the healthy newborns (n=126) as controls. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. A confidence interval that did not include the unity value of 1.0 corresponds to $p<0.05$ and was regarded as statistically significant.

Results

Morphology

Table I illustrates the severity of inflammation and the distribution of PMNs. Prevalence of PMN increased the risk for a stillbirth. For PMNs with maternal origin (in chorion plate, subchorionic fibrin layer and decidua basalis) the risk was significantly elevated; PMNs in decidua basalis was seven times as common in stillbirths as compared to controls.

Vasculitis in the umbilical cord was found in 20% of the stillbirths and 17% of the controls.

Pneumonia was found in two stillbirths. One case with villitis and cytomegalic cell changes was found among the stillbirths (cytomegalic virus infection was verified by immunohistochemistry).

Table I. Morphological findings of polymorphonuclear leucocytes (PMNs) by localization and grade in stillbirths (S) and controls (C). Odds ratio (OR) for the risk for grade 1–3 as compared with grade 0 and 95% confidence intervals (CI). Chorionic plate and subchorionic fibrin missing in one stillbirth

	Free membranes		Umbilical cord		Chorionic plate		Subchorionic fibrin		Decidua basalis		PMNs in any localization	
Grade	S	C	S	C	S	C	S	C	S	C	S	C
0	35	51	94	105	79	101	55	66	86	120	21	40
1	43	48	14	13	31	13	45	36	24	6	46	50
2	25	19	5	5	4	11	14	18	5	0	34	23
3	14	8	4	3	2	1	2	6	2	0	16	13
1–3	82	75	23	21	37	25	61	60	31	6	96	86
OR	1.6		1.2		1.9		1.2		7.2		2.1	
95% CI	0.90–2.8		0.80–1.5		1.01–3.6		0.71–2.1		2.8–21.9		1.1–4.1	

Table II. Bacteria isolated from different localization in stillbirths (S) and controls (C)

	Localization										No. of still-births with growth in organ
	Placenta		Ears		Throat	Lung	Liquor	Brain	Liver	Blood	
Bacteria	S	C	S	C	S	S	S	S	S	S	
Escherichia coli	8	1	11	14	33	5	4	4	9	3	14
Coag.neg.staphylococcus	6	18	6	40	7	5	6	1	3	0	14
Enterococcus fecalis	22	1	14	9	26	6	5	6	6	4	12
Staphylococcus aureus	3	1	4	2	5	1	3	1	2	1	3
Group B streptococcus	6	2	7	7	13	2	2	1	2	2	2
Proteus mirabilis	1	0	1	1	1	1	1	1	0	1	1
Proteus vulgaris	0	0	0	0	0	1	0	1	1	0	1
Klebsiella pneumoniae	0	0	1	0	4	1	1	0	0	0	1
Lactobacillus	1	3	0	20	0	0	0	0	0	0	0
Enterobacter cloacae	2	0	1	0	2	0	0	0	0	0	0
Alpha streptococcus	2	4	0	13	3	0	0	0	0	0	0
Pseudomonas	0	4	0	0	0	0	0	0	0	0	0
Hemophilus	0	0	0	2	0	0	0	0	0	0	0
Candida	2	0	2	9	1	0	0	0	0	0	0
Streptococcus microareofile	1	2	0	1	0	0	0	0	0	0	0
Streptococcus milleri	2	0	0	0	0	0	0	0	0	0	0
Corynebacterium	0	1	0	4	0	0	0	0	0	0	0
Group G betastreptococcus	0	0	0	0	2	0	0	0	0	0	0
Citrobacter	0	0	0	1	0	0	0	0	0	0	0
Acinetobacter	2	0	0	0	0	0	0	0	0	0	0
Enterobacter aerogenes	0	0	0	0	1	0	0	0	0	0	0
No. of subjects with growth	48	34	38	89	79	17	17	10	17	9	32
Total no. of subjects examined	115	126	116	126	116	116	115	114	115	115	116

Bacteriology

Table II illustrates the different bacteriological species isolated in cultures from different localizations.

In 60 (51%) cases bacteria were isolated in placenta and/or organs in stillbirths; in 37 (31%) cases one and in 23 (20%) cases multiple bacterial strains were isolated. The most frequent microorganisms isolated in stillbirths were *E. coli* and *Enterococcus fecalis.* Enterococcus fecalis was found in the placenta in 22 (19%) stillbirths, in one (0.8%) control (OR=30; 95% CI: 4.1–600). The same bacterial species as in placental cultures were isolated in the organs. Coag.neg. staphylococci, Lactobacilli, Alpha streptococci and *E. coli* predominate in controls, being more frequent in cultures from external ears than from placentas.

Comparison between the morphological and microbiological findings

Table III illustrates the most common bacteria isolated in placenta from stillbirths and controls. Most placentas with growth of these bacteria demonstrated chorioamnionitis. The frequency and severity of inflammatory response is presented.

Table IV illustrates associations between prevalence of chorioamnionitis and microbiological findings of the placentas. The risk for stillbirth was

Table III. Bacteria isolated in placenta and chorioamnionitis in stillbirths (S) and controls (C)

	Grade									
	0		1		2		3		Chorioamnionitis (1–3)	
Bacteria	S	C	S	C	S	C	S	C	S	C
Escherichia coli	0	0	2	0	4	1	2	0	8	1
Coag.neg.staphylococcus	0	2	5	9	1	5	0	2	6	16
Enterococcus fecalis	2	0	8	1	8	0	4	0	20	1
Staphylococcus aureus	0	0	0	0	1	1	2	0	3	1
Group B streptococcus	2	1	2	1	2	0	0	0	4	1

Table IV. Comparison between occurrence of isolated bacteria and chorioamnionitis in stillbirths (S) and controls (C). Odds ratio (OR) and 95% confidence intervals for prevalence of bacteria and/or inflammation

Inflammation	Bacteria	Bacteria isolated in placenta S	C	OR	95% CI
Present	Present	42	26	2.3	0.92–5.8
Present	Absent	53	60	1.3	0.54–3.0
Absent	Present	6	8	1.1	0.25–4.2
Absent	Absent	14	20	1	
No. of subjects		115	126		

Table V. Distribution of chorioamnionitis in macerated and non-macerated stillbirths. Odds ratio (OR) for risk for grade 1–3 and 95% confidence interval (CI)

Localization	Maceration	Grade 0	1–3	0–3	OR	95% CI
Free membranes	Yes	28	66	94	1.03	0.32–3.0
	No	7	16	23		
Umbilical cord	Yes	76	18	94	0.85	0.26–3.3
	No	18	5	23		
Chorionic plate	Yes	62	32	94	1.8	0.55–6.6
	No	17	5	22*		
Subchorionic fibrin	Yes	43	50	93*	1.3	0.46–3.5
	No	12	11	23		
Decidua basalis	Yes	67	27	94	1.9	0.56–8.4
	No	19	4	23		
Chorioamnionitis	Yes	18	76	94	0.63	0.11–2.5
	No	3	20	23		

* One case is missing.

doubled (OR=2.3; 95% CI: 0.92–5.8), if both inflammation and bacteria were present. There were 25 stillbirths and 27 controls with only slight inflammation (grade 1) at the site of membrane rupture and/or in the subchorionic fibrin. If these cases were regarded insignificant, the number of cases without chorioamnionitis and bacteria increased (25 and 49 in stillbirths and controls, respectively). The more severe the inflammatory process was, the more likely bacteria were cultured from the placentas in stillbirths, but no such correlation was seen among controls.

In stillbirths with funisitis bacterial growth in internal organs was less frequent than in those without funisitis (4/23 and 28/94, 17% and 30%, $p=0.35$).

Comparison between macerated and non macerated stillbirths

Maceration did not increase the risk for chorioamnionitis (Tables V and VI).

Meconium stained membranes

Prevalence of meconium discoloration of the free membranes increased the risk for a stillbirth in subjects with chorioamnionitis and bacteria in the placenta (Table VII). Out of 96 stillbirths with chorioamnionitis 25 had had meconium discharge but only six out of 86 controls resulting in a statistically significant OR=4.7 (90% CI:1.7–14).

Gestational age

No statistical significant difference in chorioamnionitis pattern was proven. Infarcts were more frequent among preterm (birth before 37 weeks of gestation) than term stillbirths (Table VIII).

Chorioamnionitis and placental infarcts

Deciduitis was more frequent together with infarcts than in placentas without infarcts ($N=18$; 12/31 *vs* 6/86 – $p<0.0001$) (Table VIII). Funisitis was found in 2/18 (11.2%) placentas with infarcts and in 21/99 (21.2%) without infarcts ($p=0.50$). The infarcted areas were occupying more than one third of the placental volume (Table VIII).

Discussion

There are few studies on the subject. Olding's (Uppsala, Sweden, 1966, 16) and Quinn et al. (To-

Table VI. Association between maceration and bacteria isolated in placenta, internal organ and chorioamnionitis

Maceration	Chorioamnionitis	Bacteria isolated in Placenta	Internal organ	Placenta *and* chorioamnionitis	No. of subjects
Yes	76	39	27	33	94
No	20	9	5	9	23
Total	96	48	32	42	117
p-value	0.36	0.98	0.68	0.91	–

Table VII. Comparison between subjects with and without meconium discoloration of the free membranes. Odds ratio (OR) and 95% confidence intervals (CI)

	Chorioamnionitis		Bacteria isolated in placenta		Chorioamnionitis *and* bacteria isolated in placenta		No. of subjects	
Meconium	S	C	S	C	S	C	S	C
Yes	25	6	12	5	12	4	26	8
No	71	80	36	29	30	22	91	118
No. of subjects	96	86	48	34	42	26	117	126
OR (95% CI)	4.7 (1.7–14)		1.9 (0.54–7.2)		2.2 (0.55–9.4)			

Table VIII. Comparison between preterm and term stillbirths

	Grade								
Premature	0	1	2	3	1–3	Funisitis	Chorioamniotitis *and* bacteria	Infarcts of more than 1/3 of placenta	No. of subjects
Yes	10	18	14	10	42	8	17	14	52
No	11	28	20	6	54	15	25	4	65
No. of subjects	21	46	34	16	96	23	42	18	117

ronto, Canada, 1987, 3) studies in addition to studies performed in Zimbabwe (Moyo et al. 1996, 11) and Mocambique (Folgosa et al. l997, 10) are most appropriate for comparison with our study. One study from Ireland briefly denied the role of intrauterine infection in stillbirth only on the basis of histological examination of the lungs (14). Other studies, dealing with morphology and bacteriology of the placenta, extended their investigations to prematurity (1, 5, 6, 17) or investigated only the prevalence of intrauterine infection in uncomplicated term pregnancies (12, 18, 19). Because of great variations in bacteriological techniques and different numbers of samples examined from placental tissue (from one to eight) as well as different evaluation of the inflammation by the pathologists a comparison is difficult. Bacteria were isolated in placenta in 41% of stillbirths and 26% of controls in our study. Figures from similar studies are usually lower (25% Olding; 26% Quinn et al.; 33% Moyo et al.; 28% Folgosa et al., regarding stillbirths; 7% Moyo et al., 28% Folgosa et al., 44%* Pankuch et al. regarding normal term deliveries).

Chorioamnionitis was registered in 82% of stillbirths in this study. Olding has found 71%, Quinn et al. 71%, Moyo et al. 79%, Folgosa et al. 96% in stillbirths with unexplained cause of death. The prevalence of chorioamnionitis in normal term pregnancies in our study was 68%. Varying prevalences were found in previous studies (Pankuch et al. 25%, Salafia et al. 54%, Dong et al. 85%, Moyo et al. 30%, Folgosa et al. 67%).

In our study the bacteriological findings explained the morphological chorioamnionitis in 50% of stillbirths and in 37% of controls. Interestingly, the predominating bacteria were the same as found in similar studies from developing countries: *E. fecalis, E. coli,* Coag neg Staphylococci, GBS and *Staphylococcus aureus.* More than one bacterial strain were isolated in 20%. Since GBS and *E. coli* and/or *E. fecalis* often were isolated together and from the placenta as well as from the internal organs, contamination is unlikely. There are several reasons why no bacteria were isolated in some subjects with chorioamnionitis. We did not include special growth media for fastidious agents like Mycoplasma species and Chlamydia trachomatis. Bacterial culture of the placental tissue is not the optimal site for recovering of the bacteria. Cultures from the space in between the fetal membranes seem to be more adequate (5). A slight inflammatory infiltration of the free membranes might be caused by the normal vaginal flora without subsequent spread to the placenta. The bacteria might have been killed by the inflammatory response. There may be a patchy distribution of bacteria.

In eight stillbirths and ten controls bacteria were isolated unassociated with chorioamnionitis. Some of the bacterial species are probably contaminants such as *Lactobacillus species*, alpha streptococci, *Streptococcus milleri* and Coag. neg. staphylococci. In other cases pathogens such as *Proteus species, E.coli* and GBS might have caused the death before the inflammatory response was evoked and perhaps due to toxic agents.

The high frequency of chorioamnionitis and isolated bacteria in controls is remarkable. Bacterial invasion and chorioamnionitis during the normal term delivery might be a physiological phenomenon, playing a role in the regulation of parturition,

being the cause of or the result of labor (20). The bacteria might be introduced into the uterus with seminal fluid during coitus (4). Repeated vaginal examinations may influence the vaginal flora and introduce bacteria in the uterus. Mucous plug in the cervix of pregnant women is a barrier for bacteria; therefore losing it (e.g. multiparous women) might permit the bacteria to spread freely (4).

Whether or not a microorganism will cause disease depends on its virulence and on the defence abilities of the host. That's why highly pathogenic bacteria do not cause disease in some individuals meanwhile in others bacteria of low virulence may be harmful. In our study chorioamnionitis was a common finding both in stillbirths and controls, however, with some morphological differences: inflammation in stillbirths was more frequent and more severe and an inflammatory reaction in the decidua basalis was more frequent compared to controls. The spread of infection to the decidua basalis may induce decidual necrosis due to bacterial toxins or cytokines from inflammatory cells (21). Consequent coagulation disturbances, ablatio and infarcts may occur (4). Placentas with infarcts had an increased frequency of deciduitis, which indicates that an inflammatory process in decidua basalis may trigger the development of infarcts, placental insufficiency and stillbirth. It is worth noting that in no case was the inflammation with PMNs restricted to the decidua basalis and the PMN infiltration was differentiated from the regularly appearing lymphocytes of the decidua.

Endotoxins of Gram negative bacteria such as *E. coli, Proteus* and *Pseudomonas* may cause vasodilatation, intravascular coagulation, endothelial damage and capillary exudation both in placenta and fetus. We found growth of E. coli in placenta and/or organs in 19 cases (16%) and of Proteus in two cases (1,7%) among the stillbirths.

Vasculitis of the umbilical cord and chorionic vessels is a proof of a fetal response to infection. The frequency of funisitis was equal in stillbirths (20%) and in controls (17%) in this study. The results are variable in other studies (6%* Olding, 7.9% Rayburn et al., 21% Folgosa et al. in stillbirths; 0% Salafia et al., 5% Folgosa et al., 35.8%* Dong et al. in uncomplicated term cases; 39%* Romero et al. in preterm deliveries with intact membranes) probably due to different sampling and analyzing techniques. Vasculitis of the umbilical cord occurred with the same frequency in macerated and nonmacerated children, which means that infection started before the death. Vasospasm or thrombosis of the umbilical vessels secondary to the vasculitis might cause stillbirth.

Hypoxia of the baby caused by the complications of the chorioamnionitis (infarcts, ablatio, vasculitis) may evoke meconium discharge. Naeye has found that 64% of cases with meconium in the amniotic fluid were associated with acute chorioamnionitis (4). At worst meconium is aspirated by the child and meconium aspiration syndrome is associated with high perinatal mortality (22). Altshuler and Hyde (23) exposed segments of the umbilical vein to meconium *in vitro*, and vasoconstriction occurred immediately. This may explain why the meconium exposed baby suffers from cerebral hypoperfusion (23). Meconium inhibits the intracellular killing of bacteria and phagocytosis (24) and may therefore lead to progress of infection. Intrauterine death might occur due to anoxia. The macroscopic discoloration from meconium might even have gone away at the time of examination. Meconium is phagocytized by amniotic epithelial cells and macrophages in the chorion. Only macroscopic evaluation of meconium discharge was reported in our study.

Before the 30th week of gestation the important consequence of intrauterine infection is villous edema, which, when occupying more than half of the placenta, leads to compression of blood vessels and makes fetuses hypoxic (4). In our material we found no placenta with villous edema to any important extent.

The bacterial growth in the blood and inner organs of the stillbirths means that bacteriemia and sepsis developed, which might be another cause of death. Intrauterine pneumonia was proven only in two stillbirths.

Which findings are necessary for the conclusion that acute chorioamnionitis is the cause of stillbirth? A thorough investigation including a careful postmortem with microscopy should be performed in each stillbirth excluding any other obvious cause of death.

Due to facts stated above an otherwise unexplained stillbirth with bacteria isolated in inner organs with histological chorioamnionitis reasonably has been caused by infection. This corresponds to 28/116 (24%) stillbirths in our material.

Stillbirths with growth of pathogenic bacterias in inner organs without morphological chorioamnionitis may reasonably also have died from infection. Four subjects in our material belonged to this group corresponding to further 3% of unexplained stillbirths.

Otherwise unexplained stillbirths with microscopic chorioamnionitis beyond the membranes (i.e. deciduitis, chorionitis, subchorionitis, funisitis) also without isolated bacteria might have been caused by infection. In our material these cases were 50/117 (43%).

* Figures were counted by the authors of this article.

Thus, a large part of otherwise unexplained stillbirths might be due to ascending infections also in a high socio-economic population.

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