SOME OBSERVATIONS ON CHORIO-AMNIONITIS IN PREMATURE BIRTHS

by

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Prematurity is held responsible for more neonatal deaths than any other cause. According to the Ministry of Health report on the Prevention of Prematurity (1961), in 1959 in England and Wales, 58,648 births were premature, i.e. 7.7% of all births. Fiftyfour per cent of still-births and 60% of first week deaths occurred in premature infants. The report is highly significant and requires the best efforts of all concerned to investigate the problem in detail. As regards the factors considered in the aetiology of this condition, the importance of premature rupture of membranes in the onset of premature labour has been stressed (Jeffcoate and Wilson 1956; Crosse, 1957; Bourne, 1962). The incompetent cervix has been held responsible for premature rupture of membranes (Palmer and Lacomme, 1948). An inherent weakness of the membranes has been much thought of, while other factors, such as pre-eclampsia, multiple pregnancy, anaemia, foetal abnormalities, malnutrition have been duly considered (Bourne 1962).

Infection of the foetal membranes is a rare occurrence (Benerischke and Raphael, 1958). Pathological changes in the secundies and the clinical state of both mother and her foetus apparently lack correlation (Morrison, 1952).

The present investigation was initially undertaken to examine the histological changes in the foetal membranes of both full-term and premature births, and, in doing so, attention was particularly focussed on the presence of inflammatory changes in the membranes.

Material and Methods

The material was collected from the obstetric unit of N.R.S. Hospital. Only those cases were selected who had no history of recent infection, pre-eclampsia, or gross anaemia. The material consisted of foetal membranes from both the placental site and the site of rupture. One section of membrane from the placental site, and four at 3, 6, 9 and 12 positions from the site of rupture were selected.

Each bit of membrane, measuring about 5 cm x 2.5 cm, was rolled around a match stick before fixation.

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Neutral formalin was chosen as the fixative and the tissues were processed for paraffin embedding; sections were cut at 5 μ. Besides the routine haematoxylin-eosin staining, the sections were also stained for iron (Perl's reaction), fibrin (P.T.A.H.), and PAS reaction.

Results

Foetal membranes from 50 cases of premature birth and an equal number of normal full-term births were examined.

The age-range of the mothers varied from 16 to 40 and the baby weight ranged from 2 lbs to 5 lbs 8 ozs in the premature series and 5 lbs 10 ozs to 8 lbs in the normal series. Interval between the time of rupture of the membranes and the delivery of the baby was noted in each case and the material was accordingly grouped under A, B, C, D, and E (Table 1).

The membranes were examined for the presence of (i) inflammatory reaction (ii) fibrin (iii) changes in the amniotic epithelium (iv) meconium and (v) any other abnormalities. The degree of inflammation was expressed as severe, moderate or mild, as could be assessed by the amount of inflammatory cells present either in the amnion, chorion or both. Incidence and location of inflammatory changes are presented in Table 2, while other changes are given in Table 3.

Inflammatory changes (Fig. 1-3).

These consisted of accumulation of inflammatory cells, chiefly polymorphonuclears and occasionally mononuclears. The cells were largely confined to the decidual aspect of the

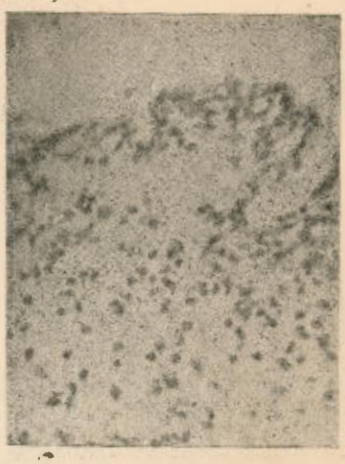

Fig. 1
Foetal membranes at the site of rupture of a case of premature birth. Shows oedema and a few inflammatory cells. H.E. x 200.

Fig. 2
Chorio-amnionitis of varying degree at the site of rupture of a case of premature birth. H.E. x 100.

membrane; in a few instances the entire chorion was involved; in some, linear streaks of inflammatory cells were found at the junction of the amnion and chorion. Amnion in most cases showed a sprinkling of the cells from the chorion below. Not infrequently the severely inflamed mem-

TABLE I

Showing Grouping of Cases According to the Duration of the Rupture of Membranes, and the Distribution of Cases According to the Severity of Inflammation in each Group

Group	Duration of rupture	Premature Series					Normal Series				
		No. in each group	Incidence & degree of inflammation				No. in each group	Incidence & degree of inflammation			
			Severe	Mode-rate	Mild	Total		Severe	Mode-rate	Mild	Total
A	0 hour to ½ hour	37 (74%)	9	9	7	25	40 (80%)	1	1	16	18
B	½ hour to 1 hour	4 (8%)	1	0	1	2	2 (4%)	0	0	1	1
C	1 hour to 2 hours	1 (2%)	0	1	0	1	3 (6%)	0	0	2	2
D	2 hours to 5 hours	5 (10%)	0	2	2	4	3 (6%)	0	0	3	3
E	5 hours to 24 hours	3 (6%)	0	2	0	2	2 (4%)	0	0	0	0
	Total	50	10	14	10	34	50	1	1	22	24

TABLE II

Showing the Incidence, Degree, and Site of Inflammatory Changes of the Membrane

Degree of inflammation	Rupture site only		Placental site only		Both rupture & placental sites		Total	
	Pre-mature	Normal	Pre-mature	Normal	Pre-mature	Normal	Pre-mature	Normal
Severe	4	1	2	0	4	0	10 (20%)	1 (2%)
Moderate	6	0	4	0	4	1	14 (28%)	1 (2%)
Mild	4	6	2	8	4	8	10 (20%)	22 (44%)

TABLE III

Showing Distribution of the Non-inflammatory Changes in the Membranes and the Associated Inflammatory Lesions

	Premature				Normal			
	Rupture site		Placental site		Rupture site		Placental site	
	No. of cases	Assoc. inflam. change	No. of cases	Assoc. inflam. change	No. of cases	Assoc. inflam. change	No. of cases	Assoc. inflam. change
Degenerative changes in amniotic epith. ..	6	3	1	1	7	3	2	1
Fibrin deposit ..	9	4	13	5	8	0	12	1
Meconium	2	0	1	1	3	1	3	1
Calcification	2	1	3	2	3	3	4	2

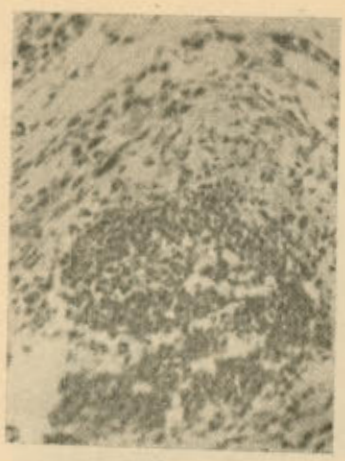

Fig. 3

Huge collections of inflammatory cells in the decidual layer of the foetal membrane of a case of premature birth. H.E. x 200.

Fig. 4

Extensive fibrin deposit in the decidual layer—two villi, one atrophic and the other calcified—are embedded in fibrin. From a case of premature birth. H.E. x 100.

branes showed micro-abscess formation. In one case in the premature series, the inflammatory cells were located around a big area of fibrinoid necrosis. More details about the inflammatory changes in both the premature and normal series are presented in Table 1 and 2.

Fibrin deposit (Fig. 4).

Varying amount of fibrin could be seen in the membranes at both the site of rupture and placental site of the premature and normal series. When present, fibrin was found to be deposited chiefly in the chorion, often separating the trophoblastic from the decidual layer. The atrophic villi could sometimes be seen embedded in fibrin mass. Membranes at the site of rupture showed fibrin deposition more frequently than at the placental site (Table 3).

Fig. 5

Amniotic fold at the site of rupture of a case of premature birth. Amniotic epithelium elongated, mush-room like. Few am. cells fused together to form giant cells. Moderate number of inflammatory cells. H.E. x 200.

Amniotic epithelium (Fig. 5).

Degenerative changes of the epithelial cells of the amnion were only infrequently seen. The changes, when present, were more at the placental site than at the site of rup-

ture. The cells were either markedly elongated, often mushroom like or tent like, or sometimes extremely vacuolated; in a few instances the entire amnion appeared as a non-nuclear band of cytoplasm. All or some of these change could be seen in a single membrane (Table 3).

Fig. 6
Few meconium-laden cells in the membrane. From a case of premature birth. Note the absence of any inflammatory change. H.E. x 200.

Meconium (Fig. 6).

Meconium appeared as dirty brown pigments giving a negative Prussian blue reaction. This was present in a few membranes, most commonly in the amnion, less so in chorion, and was found free or inside the Hofbauer cells, fibroblasts, or amniotic epithelium (Table 3).

Calcification (Fig. 7).

Deposits of calcium salts were observed in a few cases, of both the premature and normal series. Membranes at both the site of rupture and placental site showed such deposits. In most cases the atrophic villi at the upper stratum of the chorion appeared to be primarily affected (Table 3).

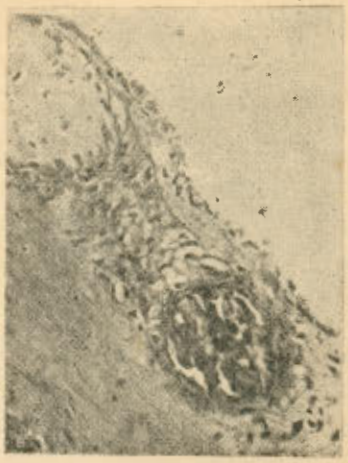

Fig. 7
Calcification of an atrophic villus. Note absence of any inflammatory reaction. From a case of premature birth. H.E. x 200

Discussion

Premature rupture of the foetal membranes has been set down as an important cause in initiating premature labour. The question which thus naturally arises is 'why such premature rupture of the membranes should at all occur'? Weakness of the membranes, either innate or resulting from inflammatory or degenerative changes, may, at least theoretically, result in early rupture of the membranes.

Tensile strength of the membranes has, therefore, been measured by different workers (Embrey, 1954, 1956; Jeffcoate and Wilson, 1956), and it has not been definitely ascertained whether such weakness at all occurs in premature births. Recent investigation of A. K. Ghose of R. G. Kar Medical College, Calcutta, has

failed to indicate any marked variation in the tensile strength of the premature and full-term membranes.

In the present investigation, membranes were selected from mothers having no history of toxaemia or any recent history of infection. The inflammatory changes observed in the membranes of these cases may thus be due to (a) an ascending infection from the vagina, (b) any irritant, e.g. meconium in the amniotic fluid, or (c) a mass of fibrin or some products of degeneration in the membranes.

It can be seen from Table 1, that in the premature series neither inflammation nor its degree is dependant on the length of the period between the rupture of the membranes and the time of delivery. In nine cases, the membranes showed intense inflammatory change even though the aforesaid interval was minimum (Group A). Conversely, inflammatory changes were present in only 2 cases where the duration was long (Group E).

It can also be seen from the same table that the incidence of inflammatory response and also its degree was more marked in the premature than in the control series. Out of a total of fifty normal full-term cases, 24 showed inflammatory response, and here again inflammation was severe in one case only. In the premature series which consisted of an equal number of cases, evidence of inflammation of the membranes was found in 34 cases, and it was severe in 10 cases. The results are highly suggestive of some factor or factors, responsible for the inflammatory changes in the membranes, particularly active in the premature group.

As is evident from the results, 22 cases of premature birth and 20 cases of the normal control group showed masses of fibrin in the chorion; inflammatory changes were, however, not frequently observed in these cases.

Calcification of the placenta is a feature in many full-term pregnancies (Wislocki and Dempsey 1946). There is no available reference to calcium deposition in the foetal membranes. In almost all instances where calcification of the membranes was observed in the present series, the salts were found deposited in the atrophic villi, and only rarely were such deposits observed outside the villi. A number of these cases with calcification of the membranes showed associated inflammatory change (Table 3).

Inflammation of the secundies has been observed to occur in response to meconium (Bourne, 1962). The pigments have been found inside the epithelial cells, Hofbauer cells and the fibroblasts of the amnion (Bourne, 1962). Presence of meconium in the membranes of the present series was not, however, always associated with chorio-amnionitis.

Degenerative changes of the amniotic epithelium were present in a number of membranes of both the premature and the control series. A concurrent inflammation of the membranes was observed in about 50% of those showing degenerative changes of the amniotic epithelium.

The present work, by itself, is not suggestive of any particular aetiological factor of chorio-amnionitis in pre-

mature birth. From the results obtained, it appears that membranes of the premature series show more frequent inflammatory changes than the membranes of the control series. It is time now to pause, and to ponder over the possible factor or factors that may initiate inflammatory changes in prematurity. And in doing so one may wonder if chorio-amnionitis is a major cause of premature birth.

Summary and Conclusions

Foetal membranes from 50 premature and 50 normal full-term births were examined for any abnormal histological change.

Evidence of chorio-amnionitis was more frequently seen in the premature than in the normal group. Severe degree of inflammation occurred in quite a number of cases of the premature group, and was rare in the normal group.

Degenerative changes of the amniotic epithelium, presence of fibrin and meconium in the membrane, and calcified areas were observed both in the premature and normal series, and the changes often showed concurrent inflammatory changes.

Chorio-amnionitis is thus observed to occur rather frequently in premature births; its aetiological relationship with prematurity can not be ignored.

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