exclude the role of the rubella virus in all cases of profound childhood deafness by means of modern virological and serological methods.

Summary

The histopathology of the embryonic and infantile inner ear following maternal rubella has been studied. This investigation has confirmed that there may be a good deal of haemorrhage present in the foetal cochlea, but this finding appeared to be absent in two of the four cases examined. The cause of haemorrhage in the foetal inner ear is not clearly understood, but we are inclined to support the view that the haemorrhage is of asphyxial origin. Furthermore, the morphological differentiation of the organ of Corti seemed to be as advanced as could be expected. The state of differentiation of the organ of Corti was normal in the two infantile cases examined. There were profound inflammatory changes in the vascular stria, representing, it is suggested, the primary lesion caused by the rubella virus followed by secondary degenerative changes in the cochlear duct and organ of Corti which would certainly have resulted in profound childhood deafness. We may therefore regard the rubella virus as capable of causing profound childhood deafness later in foetal life than formerly, or even in post-natal life.

This study has been carried out with the invaluable and skilful assistance of Miss V. F. Shepherd. The work has been aided by a grant from the Nuffield Foundation to one of us (M.I.W.), which is gratefully acknowledged. Dr. J. R. Lindsay, Director, Otolaryngology Department, Chicago University, has very kindly reviewed the sections of Case 5 which have been included in a demonstration panel of the American Deafness Research Foundation and in the demonstration "Syndromes of Deafness" from this Institute by L. Fish and C. Connolly (B.M.A. Annual Scientific Exhibition in Swansea, 1965).

The Department of Pathology and Bacteriology, the Institute of Laryngology and Otolaryngology, 330 Gray's Inn Road, London W.C.1, would be glad to receive specimens of temporal bones from cases with a history of maternal rubella or from cases where the rubella virus was isolated.

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Clotting Factors During Oral Contraception: Further Report

L. POLLER,* M.D., M.C.PATH.; JEAN M. THOMSON,† I.M.L.T.

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A rise of one of the coagulation factors (factor VII) was found to be present in women taking oral contraceptives (Thomson and Poller, 1965). This change was detected from the third month of their course onwards. The significance of the rise in factor VII activity is uncertain. Since factor VII levels are raised during pregnancy and the puerperium (Koller *et al.*, 1952), when the incidence of thrombosis is increased, and since they are raised also in patients with recent thrombosis, this may be an undesirable side-effect.

In the present study we have included data obtained from further investigation of women on a variety of oral contraceptive agents, and have sought to determine how the factor VII and other clotting changes compared with those of normal pregnancy and the puerperium. Observations were made on whether clotting changes differed in the two groups. We have studied women who have been taking oral contraceptives for longer periods to determine whether factor VII changes are cumulative.

Since our first report Hougie *et al.* (1965) have also described factor X increases in women taking one type of oral contraceptive preparation (Ortho-Novum) in the United States.

In the present paper we have therefore included additional factor X studies in oral contraceptive and control groups.

Method of Study

Oral Contraceptive Group.—Studies were performed on 97 women taking a variety of oral contraceptives (Anovlar 21, Conovid 24, Gynovlar 9, Lyndiol 8, Norlestrin 13, Ortho-novin 3, Ovulen 11, Volidan 18). Nine women had, on occasion, changed from one preparation to another. The women were tested as previously, as near as possible to their mid-cycle. They attended before the start of their course and then after one month, two months, and three months. Subsequently tests were performed between three and six months, seven and 12 months, and then between one and two years. The final group consisted of women who had been taking one or more types of oral contraceptive continuously for more than two years. The course of only one woman included in this group exceeded three years. Most of the women had in fact begun their course when their first tests were done, and were included in the appropriate group when their results were analysed on a time basis. Two women were excluded because their only tests were performed too late in their menstrual cycle, and a further woman was not included because her tests indicated

* Consultant Haematologist, Withington Hospital, Manchester.

† Research Technician, Withington Hospital, Manchester.

a haemorrhagic diathesis. The women were referred by their own doctors and by the Family Planning Clinics at our request. They were, as far as was possible, a typical cross-section of women on oral contraception, and no one with a past history of thrombosis or embolism was included.

Pregnant Group.—Tests were made on patients during normal pregnancy—13 in the first trimester, 26 in the second trimester, and 37 in the last three months of pregnancy. The post-partum group consisted of normal patients tested after delivery (mean 4.6 days).

Normal Group.—This group consisted of over 100 normal women of childbearing years. They were tested in parallel with the group of oral contraceptives and with the pregnant patients.

During the first part of the study prothrombin activities (Quick test), cephalin times, and factor VII and VIII assays were performed at each visit on the oral contraceptive group. As our first report showed no change in factor VIII levels (Thomson and Poller, 1965) these were discontinued in the oral contraceptive group and factor X studies substituted. In the pregnant and post-partum groups factor VIII assays were performed.

Technique.—The methods for prothrombin activity (Quick test), cephaline time, and factor VII and VIII assays were as described previously (Thomson and Poller, 1965).

Factor X Assay.—Method of Denson (1961) was used. The results were expressed in seconds.

Results

Results of assays in the different groups are given in Tables I–III. Results of prothrombin activity have not been included because they showed no significant variation throughout.

Cephalin Times.—There was still no significant difference in cephalin time between the oral contraceptive and the normal group. In contrast, the pregnant patients showed progressively shorter cephalin times, which became significantly shortened during the second trimester, the most marked acceleration occurring post-partum. On the other hand, results in the

TABLE I.—Results in Normal Control and in Women on Oral Contraceptives

	Normal Controls			Women on Oral Contraceptives		
	Total	Mean (Time sec.)	S.D.	Total	Mean (Time sec.)	S.D.
VII assay	112	18.85	1.54	170	18.05	1.91
Cephalin	122	65.12	1.48	196	64.14	1.98
A.H.G. { 10%	53	18.2	1.31	60	18.1	3.2
{ 20%	53	15.1	1.12	60	15.0	2.5
{ 30%	53	14.3	1.37	60	14.6	1.6
X assay	27	18.5	1.11	52	17.4	1.12

TABLE II.—Results in Women on Oral Contraceptives According to Duration of Course

	Total	Mean (Time sec.)	S.D.
0 week			
{ VII assay	23	18.9	1.77
{ X	9	18.8	0.6
{ Cephalin	23	66.0	1.72
1 month			
{ VII assay	15	18.4	1.5
{ Cephalin	15	64.0	1.96
2 months			
{ VII assay	13	18.8	1.4
{ Cephalin	13	63.7	1.92
3 " (1–3 months)			
{ VII assay	18	18.0	1.5
{ X	18	18.0	2.04
{ Cephalin	18	64.3	2.24
4–6 "			
{ VII assay	35	17.7	2.2
{ Cephalin	36	63.9	1.35
7–12 "			
{ VII assay	38	17.8	1.46
{ X	10	17.1	1.18
{ Cephalin	39	65.0	2.0
> 12 "			
{ VII assay	9	17.1	1.89
{ X	7	16.9	0.41
{ Cephalin	14	64.4	1.6
> 2 years			
{ VII assay	18	16.1	1.1
{ X	15	17.4	1.5
{ Cephalin	19	65.5	1.31

TABLE III.—Results in Pregnant and Post-partum Groups

	Total	Mean (Time sec.)	S.D.
Antenatal Group			
0–12 weeks			
{ VII assay	13	19.38	2.27
{ Cephalin	13	64.46	2.94
{ A.H.G. { 10%	13	17.3	2.79
{ 20%	13	14.6	2.02
{ 30%	13	13.1	1.43
{ X assay	12	18.6	0.30
13–24 "			
{ VII assay	26	17.17	0.96
{ Cephalin	26	63.42	3.72
{ A.H.G. { 10%	24	17.91	3.01
{ 20%	24	15.0	1.7
{ 30%	24	13.56	1.07
{ X assay	16	17.7	1.04
25–36 "			
{ VII assay	37	16.16	0.78
{ Cephalin	37	61.59	2.53
{ A.H.G. { 10%	27	14.5	1.28
{ 20%	27	13.14	1.15
{ 30%	27	12.33	0.93
{ X assay	15	15.6	0.87
Post-partum Group			
VII assay	26	16.73	1.23
Cephalin	21	59.5	1.66
X assay	27	16.9	1.31

pregnant patients only became significantly shorter than the oral contraceptive group during their third trimester.

Factor VII Assays.—When the total group on oral contraceptives was compared with the normal controls there was a significant increase in factor VII. On a time basis, months 1 and 2 showed no significant change. The rise in factor VII levels became significant only from the third month onwards. The difference was progressively greater, with the maximum in those patients who had been on oral contraceptives for more than two years. In the pregnant patients there was no significant rise in factor VII levels in the first trimester, but these became significantly elevated in the second trimester; maximum factor VII activity was recorded during the third trimester. Levels fell post-partum but were still significantly raised. When the first trimester of pregnancy was compared with the first three months on oral contraceptives there was no significant difference, nor was there significant difference in the second trimester compared with the second three months of their contraceptive course. Only in the third trimester did the pregnant group show a significant rise over a comparable period on oral contraceptives. After two years, however, the rise in factor VII levels in patients on oral contraceptives was comparable with the third trimester of pregnancy. Results in the post-partum group showed less factor VII activity than in women who had been on "the pill" for two years, but the difference did not quite reach the significance level.

Factor VIII Assay (Antihaemophilic Globulin).—There was no significant rise in A.H.G. levels during the first trimester of pregnancy, but from the second trimester onwards a significant rise was recorded.

Factor X.—A significant increase in factor X levels was found in patients on oral contraceptives compared with the normal group after three months. Results during pregnancy were significantly raised from the second trimester onwards. The pregnant women showed significant rise only in the third trimester, but the results in the oral contraceptive group never became of a similar order to those in the latter stages of pregnancy.

Discussion

Further study has again revealed increased factor VII activity after oral contraceptives. The present study was weighted by an increased number of women who had received longer courses, and, unlike the first report, the whole group showed raised factor VII activity. The first two months again showed no significant change.

The factor VII rise in the last trimester of pregnancy exceeded that of a similar period on oral contraceptives, but after two years the oral contraceptive group showed changes of the same order.

The clinical significance of raised factor VII levels is not certain, but we have shown increased levels in patients with recent thrombosis (Poller, 1957; Thomson and Poller, 1965). Similar changes during pregnancy and the puerperium have been regarded as evidence of a thrombotic tendency. The worrying feature is that increasing duration of oral contraception appears to result in proportionately raised factor VII levels.

The raised factor X activity confirms the findings of Hougie *et al.* (1965), but did not seem as great in the oral contraceptive groups when compared with pregnancy. So far there is no evidence that the factor X rises are cumulative.

The changes in pregnancy appeared to be more pronounced than in the oral contraceptive group, but factor VII levels rose to a similar extent after two years, and the duration of the cumulative effect is not yet known.

Summary

A further report on coagulation studies on a group of women taking a variety of oral contraceptives confirms the presence of increased factor VII activity from the third month of their course. With the inclusion of results from women who have had longer courses the whole group now shows significantly

increased factor VII activity. There is new evidence that the effects on factor VII may be cumulative. In addition, a significant rise in factor X was detected in the same group from the third month onwards, though the changes were not so great.

A broader spectrum of clotting tests appeared to be accelerated during normal pregnancy than during oral contraception, and both factor VII and X levels were higher when comparing trimesters of pregnancy with a similar period on oral contraceptives. After a two-year course the rise in factor VII levels was of the same order. It is important to determine whether factor VII goes on increasing with more prolonged courses of oral contraception.

We are grateful for the cooperation of the practitioners in the South Manchester Area, and the Manchester Family Planning Clinic. We are indebted to Dr. M. C. G. Israëls for supplies of factor-VIII-deficient plasma used in our assays, and to the Manchester Regional Hospital Board for a grant for thrombosis research.

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Colostomy Management by the Irrigation Technique: Review of 165 Cases

P. W. SEARGEANT,* F.R.C.S.

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For many years people have argued over the relative merits of the two main methods of colostomy management—namely, colostomy wash-outs by patients or management by dietetic means. Grier *et al.* (1964) had rather disappointing results from an interrogation of some 50 colostomy patients being managed on the dietetic regimen at a variety of hospitals.

Present Investigation

There seems to have been no comparable survey of patients who have been taught to manage their colostomies by the irrigation technique. It was therefore thought worth while to carry out a survey (in 1963) of all the colostomy cases assumed to be living at this date, and whose abdomino-perineal excisions of rectum had been performed at the Gordon Hospital. For this purpose the following questionnaire was sent to 216 patients:

1. How long have you had your colostomy?
2. How often do you wash it out?
3. What time of day do you do your wash-outs?
4. How long does the wash-out take (including cleaning the apparatus)?
5. Does it work between wash-outs?
6. Are you able to lead a normal life?
7. Are you able to eat normal food?
8. Do you ever wear any form of colostomy bag?
9. Have you ever had any complications with your colostomy?
10. Do you ever take anything for your bowels?

Of the 216 patients three had died within the previous few months, one had emigrated, and 47 could not be traced (13 changed addresses), leaving 165 who replied, some at great length. It is upon the answers of these patients that observations are made.

* Consultant Surgeon, West Norfolk and King's Lynn General Hospital, King's Lynn, Norfolk.

Table I shows the number of years that patients have had their colostomies. It soon became apparent that, despite their original training, some patients had ceased to wash out their colostomies altogether for various reasons, ranging from old age to the advice of friends, while others were washing out at various intervals other than daily. Table II shows the distribution

TABLE I.—Number of Years Patients had Colostomies

Years since Operation:	1	2	3	4	5	6	7	8	9	10
No. of patients	6	20	12	17	6	16	9	11	7	13
Years since Operation:	11	12	13	14	15	16	17	18	19	20+
No. of patients	18	7	9	6	3	1	1	0	0	3

TABLE II.—Frequency of Wash-outs

Not at All	Once Daily	Alternate Days	Every Third Day	Once a Week	Five Times a Week (Not at Week-ends)	Rarely
34	113	7	4	3	3	1

of patients according to their frequency of wash-outs. Linked with this is the question of whether the colostomy functions between wash-outs or not. In 47 patients it did not function, in 58 it rarely functioned, and in 23 it occasionally functioned.

This accounts for 128 of the 165 cases reviewed. The remaining 37 cases included 34 who ceased wash-outs either of their own accord, usually because of old age and infirmity, or on the advice of other hospitals, and three who failed to answer this particular question.

Before proceeding further an analysis of the 23 patients whose colostomy "misbehaves" itself is of interest. They were distributed as follows: