matrix, which is flexible enough to allow the fibrils to show their elasticity due to changes in orientation.

The experiments undertaken show that with advancing age, beginning at the end of the third decade, there are changes in the collagen structure of both nucleus pulposus and annulus fibrosus which affect both factors.

The nucleus loses its gel properties, as seen by the increased orientation and crystallization of the collagen with advancing age, whilst the collagen of annulus fibrosus undergoes similar changes, the fibrils being laid down in a uniaxial arrangement which inhibits its elastic mechanism. In these circumstances the intervertebral disk loses its normal physiological function, with secondary effects upon its associated spinal joints, particularly impaired mobility.

Summary

The collagenous changes in the human intervertebral disks with age have been studied, using x-ray crystallographic methods.

The x-ray diffraction diagrams so obtained prove that the elasticity of the annulus fibrosus is dependent upon the orientation and mobility of the collagen fibrils, properties which decrease with advancing age after the third decade.

The x-ray diffraction diagrams of the nucleus pulposus show that increased orientation and ultimate crystallization of the collagen occurs with advancing age, indicating loss of gel structure and hence impaired elasticity.

The combination of these factors will explain the reduced elasticity of the intervertebral disk with age.

Financial assistance from the Wool Textile Research Council for part of this work is gratefully acknowledged.

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SERUM ANTITHROMBIN CONTENT IN PREGNANCY

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In a follow-up examination of adult cases of coeliac disease the serum antithrombin content estimation was used as a screening test to exclude fibrocystic disease of the pancreas as a possible alternative diagnosis. The results were normal in all cases but one—that of a woman three months gravid. Sera from six other pregnant women were then examined, and since in each case the antithrombin content was found to be much lower than that of normal serum the investigation now reported was undertaken.

Sera were obtained from 120 women whose pregnancy varied from four weeks to full term; from 41 women whose delivery had been from one to twelve weeks previously; from cord blood at 30 births; and from 15

babies aged 1 to 14 days. All pregnancies were normal and the sera were obtained from routine laboratory collections. The babies from whom blood was obtained were likewise normal and full-term. The Table shows the distribution of these sera. The antithrombin content was estimated in every case. The technique

Details of the Sera Examined and the Results Obtained, Expressed as a Percentage of the Normal Mean

Sera	No.	Antithrombin Content			Sera	No.	Antithrombin Content		
		Max.	Min.	Mean			Max.	Min.	Mean
Pregnancy:					Post Partum:				
4-7 weeks	3	72	60	67	1-4 weeks	28	62	18	35
8-11 "	9	66	26	50	5-8 "	4	106	65	90
12-15 "	24	58	22	35	9-12 "	9	107	89	100
16-19 "	9	45	22	32					
20-23 "	10	48	23	34	Total	41			
24-27 "	11	41	22	33					
28-31 "	23	52	22	35	Babies:				
32-35 "	11	48	20	36	Cord blood	30	58	20	32
36-39 "	16	41	18	29	Newborn				
Full term	4	41	22	32	(1-14 days)	15	64	26	40
Total	120								

employed has already been detailed by one of us (MacFarlane, 1952) and is a modification of the original method described by Innerfield *et al.* (1951). Briefly, the test consists of the incubation in a water-bath at 37° C. of a standard solution of thrombin mixed with the serum to be tested, and the timing of the clotting of standard amounts of normal citrated plasma by this thrombin-serum mixture after 5, 10, 15, and 20 minutes' incubation. The clotting times of each sample are expressed as a percentage of those obtained using normal serum as a control, normal and abnormal being tested concurrently.

Results

In the assessment of the results obtained the percentages of the normal of the 20-minute sample of the thrombin-serum mixture only are considered, for in this sample any deviation from the normal is most marked. We have used the same technique over a period of more than two years: the variation in clotting time of some 800 "normal" sera in this 20-minute sample was from 90 to 110% of the mean of each batch of normals tested, and we have come to regard any figure of less than 80% as being pathological. The Chart shows the scatter of the results obtained on examination of the 120 sera taken during pregnancy and of the 41 sera obtained post partum, while the Table also lists the highest, lowest, and mean result obtained in each four-weeks period. It will be seen that from the fourth week of pregnancy onwards the serum antithrombin content is reduced to an abnormal degree. The mean of the three sera tested in the fourth to seventh week of pregnancy is 67%; that of the nine sera in the eighth to eleventh week is 50%; and the means of the sera belonging to the succeeding four-weeks periods to full term all lie around 35% of normal. After delivery the antithrombin content remains low for several weeks, certainly for as long as four weeks, for the highest figure of this group of 28 sera was 62%, with a mean of 35%. Somewhere between five and eight weeks post partum the results return to normal in the majority of cases, three of the four sera in this period tested being normal, while from the ninth week onwards all nine sera tested gave normal results.

All 30 sera obtained from cord blood gave abnormally low results, varying from 20 to 58% of normal, with a mean of 32%. The sera of the babies 1 to 14 days old also showed an antithrombin content much lower than that of normal serum, the mean here being 40%. In the routine investigation to exclude fibrocystic disease of the pancreas the antithrombin content has been within the normal limits in the serum of all the 2-months-old normal babies tested.

Chart showing the scatter of results during pregnancy and the post-partum period.

These results are included, although they have no direct bearing on pregnancy, because they are interesting, and because they may throw some light on the possible explanation of the low antithrombin levels found in pregnancy. Obviously more investigation of the sera of the newborn is necessary.

Discussion

The results seem to indicate that the serum antithrombin titre offers a simple and reliable aid to the diagnosis of pregnancy in difficult cases, probably from as early as the fourth week, and certainly from the eighth week onwards. It is not in any way suggested that this test should supplant the well-proved animal tests in present routine use, though it seems to have certain advantages. In the investigation of uterine bleeding following amenorrhoea it might be of considerable assistance, however, for, whereas the biological tests give normal results very rapidly after abortion or miscarriage, the results here recorded indicate that the antithrombin content of the serum may remain low for several weeks following such an occurrence.

The test is easily executed, requires no complicated apparatus or reagents, and can be carried out on blood obtained from a finger-prick, for the test employs only 0.1 ml. of serum. It must be emphasized that it is essential to compare the serum to be tested with at least one normal control, tested concurrently, for, as has been stressed by MacFarlane, no absolute comparison is possible for technical reasons between the results obtained in one batch and those obtained in another.

The examination of more than 800 "normal" sera while investigating the results in fibrocystic disease of the pancreas has given only six "false-positive" results. These six patients suffered from chronic eczema, miliary tuberculosis, and acute exacerbations of chronic respiratory disease (four cases). The error in normal sera is therefore apparently less than 1%, and even the "errors" occurred in patients quite obviously ill. It is interesting to note in passing that the

results obtained from the five cases of respiratory disease became normal within four to eight weeks of the response of the complaint to treatment. Similarly, too, in the three cases of acute pancreatitis investigated, in which the patients recovered following operation, the low levels encountered at the onset of the disease returned to normal seven, nine, and thirteen weeks respectively after operation. Otherwise fibrocystic disease of the pancreas was the only condition found in which the antithrombin level of the serum was low. In children with this disease a lowered serum content was found in 106 of the 118 proved cases investigated; in this condition the level remains low despite treatment.

It would be pleasant to be able to offer some definite rationale for these results, in pregnancy as in the other conditions in which a low titre was found. To exclude a simple hormonal change in pregnancy the sera from eight female laboratory technicians were examined weekly for a period of ten weeks. The results all lay within normal limits and the menstrual cycle produced no variations in any case. A specious theory regarding the cause of the low levels found in fibrocystic disease of the pancreas and acute pancreatitis could be based on the simple fact that the addition of a minute amount of crude trypsin (as a high dilution of liq. trypsin co.) to normal serum produces a very low antithrombin titre in the normal serum. In both these conditions it is possible that there is an excess of trypsin in the blood, this excess producing the lowering of the antithrombin content of the serum. It might be suggested that the enzymes known to exist in the developing, and possibly even in the ageing, placenta likewise produce a lowering of the antithrombin content of the serum of both mother and child during pregnancy. The effect on the level in the blood of both foetus and mother and the cessation of the influence in both shortly after parturition seem to point to the cause lying in the placenta. The absence of any concrete evidence in support of this theory does not, however, influence the use of the test as an empirical aid to the diagnosis of pregnancy.

Summary

In 120 cases of pregnancy, varying from four weeks' duration to full term, the serum antithrombin level in every case has been found to be much lower than that of normal serum. The examination of 41 sera obtained post partum shows that the titre remains low for at least four weeks but returns to normal some time between five and twelve weeks after delivery.

It is suggested that the test may be useful as aid to the diagnosis of pregnancy in certain obstetric problems.

We are indebted to Dr. J. Murray, Director of the Pathology Department of Queen Charlotte's Maternity Hospital, London, for supplying the sera from pregnant and post-partum women and for the cord bloods; to Dr. C. Upjohn, of St. Helier Hospital, Carshalton, for supplying the sera from the newborn; and to Mr. G. W. Cecil, for much expert technical assistance.

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"Every scholarly discipline breeds its own jargon . . . jargon is a legitimate form of short-hand conveying in a phrase several related ideas, but too often a deep-seated mental laziness pervades the scholar who uses it as *cliché*. He also uses it as a drug to deaden his fears. He longs for anonymity, an anonymity which protects him from the biting attacks of other scholars. If he can reduce his own personality to the smallest proportions by employing such terms as 'the present writer,' by using verbs in the passive rather than the active tense and by eliminating every sign of an individual having written the work, he hopes his critics will not notice that he has written it" (*The Times Literary Supplement*, July 16, p. 458).