lateral femoral condyle. When fibrillar cartilage was taken from the patellar surface of the femur, healthy cartilage was also removed from an adjacent area. Cartilage from the weight-bearing areas of the medial and lateral condyles and from the patellar surface of the femur of healthy adult knee-joints without fibrillation served as a further control. Cartilage samples obtained in this way were finely divided with a scalpel, dehydrated in several changes of acetone, and finally dried over concentrated sulphuric acid *in vacuo* to constant weight. Determinations of collagen and chondroitin sulphate on aliquots were carried out as previously described (Matthews, 1952).

Results

The accompanying table gives results obtained from seven knee-joints showing twelve comparisons between fibrillar and healthy cartilage. Five joints showed lesions of both medial condyle and patellar surface, while in two the medial

Collagen and Chondroitin Sulphate Content of Fibrillar and Healthy Articular Cartilage in the Knee (% of Dry Weight)

Case	Age	Hydroxy- proline as Collagen	Hexosamine as Chondroitin Sulphate	Collagen/ Chondroitin- sulphate Ratio	Mean of Ratios	Hydroxy- proline as Collagen	Hexosamine as Chondroitin Sulphate	Collagen/ Chondroitin- sulphate Ratio	Mean of Ratios
Fibrillar Cartilage: Weight-bearing Surface of Medial Femoral Condyle						Healthy Cartilage: Weight-bearing Surface of Lateral Femoral Condyle			
1	42	53.3	13.2	4.0	} 3.67 s.d. 1.18	45.0	21.6	2.1	} 2.09 s.d. 0.33
2	49	62.3	14.8	4.2		52.5	20.8	2.5	
3	64	56.3	20.0	2.8		50.3	26.0	1.9	
4	68	51.8	20.0	2.6		45.0	23.2	1.9	
5	68	62.3	10.4	6.0		54.0	22.0	2.5	
6	78	52.5	16.8	3.1		45.8	21.6	2.1	
7	81	47.3	15.6	3.0		44.3	27.6	1.6	
5 control cases with- out fibril- lation aged 45-75	Weight-bearing surface: medial femoral condyle				1.94 s.d. 0.09	Weight-bearing surface: lateral femoral condyle			2.10 s.d. 0.07
Fibrillar Cartilage: Patellar Surface of Femur						Adjacent Healthy Cartilage: Patellar Surface of Femur			
1	42	60.0	15.7	3.8	} 5.16 s.d. 2.54	48.0	20.4	2.4	} 2.34 s.d. 0.20
3	64	57.8	18.4	3.1		54.8	22.0	2.5	
4	68	50.3	8.4	6.0		53.4	21.5	2.5	
5	68	60.8	9.2	6.6		53.2	23.0	2.3	
6	78	60.8	9.6	6.3		50.2	25.0	2.0	
5 control cases with- out fibril- lation aged 45-75	Patellar surface of femur				2.12 s.d. 0.07				

condyle only was affected. Additional results obtained from five control subjects whose ages ranged from 45 to 75 years, and in whom there was no evidence of fibrillation within the knee, are included.

It is evident that in fibrillar lesions of articular cartilage in the knee the collagen/chondroitin-sulphate ratio is greater than in healthy cartilage from the same joint; the ratios obtained for the latter agree well with those found for comparable sites in healthy joints.

The water content of the samples analysed was not determined. This value was readily obtained for smooth, healthy articular cartilage; but in fibrillar material, where a variable amount of extraneous water is held in the interstices, the true state of hydration is difficult to determine.

Discussion

The present-day morphological concept of fibrillation gains support from chemical analysis: the increased collagen/chondroitin-sulphate ratios found (as compared with healthy cartilage) reflect chemically the different rates of loss of these substances in cartilage undergoing fibrillation. As continued loss of cartilage tissue occurs, the more durable collagen fibres, though architecturally deranged, are lost at a slower rate than matrix substance. Although to the naked eye the areas of fibrillar cartilage analysed were of approxi-

mately similar severity, the ratios showed marked variation. Histological evidence of variation in the degree of fibrillation could not be obtained because the entire material removed was needed for analysis. It is conceivable, however, that, as the fibrillation process evolves, the extent to which intercollagenous matrix is lost is variable from lesion to lesion.

Fibrillar lesions of cartilage are an expression of injury (Collins, 1949). Though it cannot be stated that fibrillation is initiated by mechanical factors alone, it is clear that once a breach has occurred in a smooth articular surface they then become potent pathogenic stimuli. The results reported therefore throw no light on the earliest chemical changes which must occur in articular cartilage before even incipient evidence of fibrillation appears.

While the nature of this early change remains unknown, it is reasonable to suggest that it primarily involves chondroitin sulphate. Thus Benninghoff (1925a, 1925b) concluded from histological studies that depletion of matrix (containing chondroitin sulphate) renders the superficial cartilage and its bared fibrils vulnerable to pressure, permitting the development of both circumscribed defects and generalized flattening. In normal cartilage Hirsch (1944) has emphasized the importance of chondroitin sulphate in maintaining elasticity; and Matthews (1952) has shown that in normal weight-bearing or mechanically stressed cartilage the proportion of chondroitin sulphate is increased. Conversely, in patellar articular cartilage undergoing fibrillation, loss of resilience is accompanied by a diminution in mucopolysaccharide content (Hirsch, 1944). Once initiated, the evolution of fibrillation is the result of a vicious circle in which loss of chondroitin sulphate leads to decreased resilience, which in turn facilitates the mechanical perpetuation of the process.

I wish to thank Dr. E. G. L. Bywaters, who suggested this work, and Dr. L. E. Glynn and Dr. R. Consden for their help and guidance.

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Medical Memoranda

Diabetic Coma Associated with Lipaemia and Complicated by Uraemia

Although many cases of lipaemia associated with diabetic coma have been reported, the following case is of interest because of the marked degree of lipaemia attained, with the manifestation of lipaemia retinitis, and also because of the unusual feature of temporary kidney dysfunction.

CASE REPORT

A married woman aged 22 was admitted to hospital on August 9, 1951, deeply unconscious, with a history that, since an apparently normal pregnancy ten months previously, she had been complaining of weakness, and for the past three weeks of loss of weight and polyuria. She had been unconscious for about ten hours before admission.

On examination the patient could not be roused by painful stimuli. Her temperature was subnormal. A pustular rash was present over the extensor surfaces of the knees and elbows, consisting of raised yellowish white nodules, 2 to 3 mm. in diameter, with an erythematous periphery. Her blood pressure was 70/50. The pulse was 102 regular, and of fair volume. The pupils were small and reacted equally to light; corneal reflexes were absent. All tendon reflexes were absent. The extremities were flaccid. Fundi: the disks were normal; all vessels presented a waxy-white

appearance with the vessel walls clearly defined. No abnormalities were found in the respiratory system or gastrointestinal tract.

Investigations.—Haemoglobin, 61% ; W.B.C., 26,000 (5,200 monocytes). Urine contained albumin, and the sediment showed scanty granular casts. Benedict's test, orange. Rothera's test, strongly positive. Blood sugar, 600 mg. per 100 ml. ; blood urea, 50 mg. per 100 ml. In view of the appearance of the fundi, which were strongly suggestive of lipaemic retinitis, the following investigations were carried out : serum free cholesterol, 220 mg. per 100 ml. ; serum ester cholesterol, 710 mg. per 100 ml. ; serum total lipoids, 7.84%. The blood serum was of a whitish, opalescent, milky appearance, and became solidified as it cooled to room temperature. Lumbar puncture : despite the fact that the cerebrospinal fluid was cytologically and biochemically normal, apart from an elevated sugar fraction, it also presented an opalescent slightly "milky" appearance.

An intravenous drip of normal saline was started, and intravenous insulin given, 1,600 units during the first five hours, after which she became conscious of her surroundings and was able to answer simple questions, though she remained very drowsy, with marked hyperventilation. Her blood sugar was 480 mg. per 100 ml. The next day there was no material change in the level of consciousness, and hyperventilation was still in evidence. An electrocardiogram showed pronounced inversion of the T waves in leads I and CR₄, which, together with her continuing hypotension, was regarded as indicative of hypopotaemia. Potassium was given by mouth and her general condition greatly improved, though the serum potassium twenty-four hours later was still only 15.7 mg. per 100 ml. By this time her E.C.G. tracings were normal and her blood pressure had risen to 110/80. Great disparity was observed between the blood and urinary sugar levels. Although her blood sugar was at times almost 600 mg. per 100 ml. there was never more than 1% sugar detectable in the urine, and quite often the urine proved to be sugar-free. Further, her output of urine was very small, and her blood urea steadily rose to a maximum of 180 mg. per 100 ml. nine days after admission, with gradual deterioration in her general condition.

Treatment was continued, her daily requirements of insulin, given with reference to frequent blood-sugar estimations, remaining very high. Her blood-urea level persisted unchanged for the next 10 days, after which it slowly declined to normal, accompanied by an increase in urinary output, the disappearance of the hyperlipaemia, a return of the renal sugar threshold to normal, and much improvement in her general condition. Her ultimate requirements of insulin proved to be 30 units a day. On discharge, after nine weeks in hospital, her blood urea was 35 mg. per 100 ml. and serum total cholesterol 213 mg. per 100 ml.

When seen six months after discharge her condition remained satisfactory.

We would like to thank the Department of Pathology, Dudley, Stourbridge, and District Group, for the investigations made on this patient.

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Torsion of the Gall-bladder

Torsion of the gall-bladder seems to be rare enough to warrant the recording of a further case. Only about 80 cases have so far been reported in the literature since Wendel's original description in 1898, and most of these were in foreign countries. Rendle Short and Paul (1934) found only 50 cases, to which they added three. Krabbel (1920) and Kettner (1930) reported a correct pre-operative diagnosis in each of their two cases, but in spite of the striking clinical picture others do not seem to have emulated their example. A prerequisite of the condition is an unusual anatomy of the gall-bladder, surrounded on all sides by peritoneum and hanging free in the peritoneal cavity by a mesentery attached to the anterior border of the liver. Caldwell (1950) makes arteriosclerosis a possible additional

predisposing factor in that the cystic artery may become tortuous and encourage rotation of the organ.

The twist is either clockwise or anti-clockwise. It has been suggested that, if the former, peristalsis of the colon may be responsible ; if the latter, then peristalsis of the stomach may initiate the rotation. The age incidence is from 11 to 84 years, but most of those suffering torsion have been between 60 and 80. The clinical picture is very striking, and the case recorded followed the usual pattern except that no mass was felt.

CASE REPORT

A married woman aged 65 was admitted at 9.30 p.m. on September 5, 1951, with severe colicky abdominal pain. She had been well until 8 p.m., two days previously, when she complained of the sudden onset of right-sided abdominal pain, and vomited. The pain was felt in the R.I.F., and there had been colicky exacerbations of intensity. From the onset of the pain until admission she vomited four times. Since the pain had started there had been constipation and anorexia. She complained of right shoulder pain, for one hour only, prior to admission. There was no urinary upset.

Her temperature was normal and pulse rate 82. Examination of the abdomen revealed extreme tenderness from the region of McBurney's point upwards towards the right hypochondrium. The patient would scarcely allow the abdomen to be touched, but there was no rigidity. No mass was felt. Rectal examination revealed nothing abnormal. A diagnosis of acute appendicitis was made, and the abdomen was first opened by a gridiron incision not long after admission. There were many adhesions in the region of the appendix, but that organ showed no signs of recent inflammation. Appendectomy was performed. In the upper angle of the wound a globular cystic swelling was palpated, and when a retractor was put into position this swelling was found to be black and running upwards as far as could be felt or seen. Gangrene of the gall-bladder was assumed and the abdomen was closed in the R.I.F. and reopened by a right Kocher's subcostal incision. A gangrenous gall-bladder was confirmed, and the cause was found to be torsion at its neck by one and a half turns in an anti-clockwise direction. The twist was reduced and an easy cholecystectomy performed. The organ was found to have its wall grossly thickened by oedema and contained an almost black fluid. A drainage tube was passed down to the ligated cystic duct and the abdomen closed.

The patient made an uninterrupted recovery, and was discharged on the twelfth post-operative day.

Pathological Report.—"Specimen of gall-bladder received with black oedematous walls measuring 4½ by 2 by 1½ in. (11.4 by 5 by 3.8 cm.). The wall was soft and spongy, and was ¼ in. (6 mm.) thick. The gall-bladder showed no evidence of previous inflammation, though a few small gritty pigment stones were present. Sections were taken of the neck of the gall-bladder, together with the cystic artery, and another of the artery itself just distal to the site of ligation. The histology showed complete infarction of the gall-bladder and the artery showed no atheroma."

I discussed this case with Mr. S. Chambers, then senior surgeon to the hospital, and he told me that he had seen two such cases in his 30 years as surgeon at the hospital. The last one occurred eight months previously.

I have since heard from Mr. Raymond Purvis that in July, 1946, he operated on a woman aged 84 whose torsion came on while she was sitting quietly in a chair.

I wish to record my thanks to Mr. R. Purvis, surgeon to the Royal South Hants Hospital, for permission to publish this case, admitted to one of his beds in the hospital.

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