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Thesis for the degree of M.D.

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Chemical investigations on the degenerative changes in diseased bone (conducted in the Pathological Chemical Laboratory at the Western Infirmary), with remarks on excision of joints.

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The investigations, the results of which are given in the following pages, have not so much on the changes in the ultimate chemical composition of diseased bone as on the inflammatory, or rather degenerative, processes which occur in the organic tissues of bone, chiefly in the inflammation of bone which occurs in the neighbourhood of diseased joints preliminary probably to caries, and in necrosis. The results of earlier analyses than those given here directed special attention to the proportion of fatty matters present, and special care has been taken by improved method and apparatus to ensure that the results bearing on that point are reliable.

The fresh bones were submitted to analysis as soon as possible after removal from the body by operation, without washing, boiling, or maceration, or indeed any preparation beyond careful re: : moval of the cartilages and ligaments, so that

the results represent, as nearly as may be, the state of the bone in the living body.

I hoped to have been able to compare these results with those of microscopical examination, but as circumstances will prevent my fulfilling my intentions for some time at least, I am compelled to give only the chemical data.

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The analyses from pp. 4 to 15 show —

A. The proportion per cent of organic solids (nitrogenous and fatty), salts, and water. A very considerable proportion of the water, and a small amount of the nitrogenous tissue must be credited to blood in the bone.

B. The proportion per cent of organic solids (nitrogenous and fatty), and salts, when the water is deducted; i.e. in dried bone.

C. The proportion of nitrogenous and fatty matter in every 100 parts of organic tissue of the bone.

Index.

The tables on p. 4 is from a comparatively early stage of Osteo-myelitis in the proximity of a diseased joint; those on p.p. 5, 9, 10, 11, 13 and 15 are from specimens of the same affection at a much later stage; a summary of these later is given at p. 16.

The tables on pp. 6, 8, and 12 are from cases of necrosis, and are summarised in the table on p. 17.

The table on p. 7 is from a specimen of bone removed post-mortem from a case of pernicious anæmia.

The table on p. 14 is from a specimen of presumably normal bone.

General comparative tables are given on p.p. 18 and 19, and 20.

The nature of the pathological processes leading to caries & necrosis is described pp. 21 to 26, and the clinical bearings are discussed from p. 27 to the end.

Analysis 1.

4·226 grammes. Portion of humerus from excised elbow joint. The bone medullary and but not softened. Cartilage normal in appearance and firmly attached to the bone.

A. Organic solids. nitrogenous. 39·115
Fatty ——— 11·192
50·307.
Salts ——————— 27·163
Water ——————— 22·290.

B. Organic solids. nitrogenous. 50·490
Fatty ——— 14·446
64·936
Salts ——————— 35·062

C. Nitrogenous solids - 73·7
Fatty ——— 26·3.

Analysis 2.

9·905 grammes. From condyle of femur removed in an excision of the knee joint. Bone yellow, very soft, cutting easily with scissors. Cartilage yellow and stripping off easily, but not ulcerated.

A. Organic solids. Nitrogenous 17·324
Fatty — 52 82·094
69·418
Salts — 9·932
Water — 20·646

B. Organic solids. Nitrogenous 21·805.
Fatty — 65·650
87·495
Salts — 12·576

C. Nitrogenous solids 24·957.
Fatty substances 75·043.

Analysis 3.

2.354 grammes. Spicule of necrosed bone from the lower end of the tibia, from an amputation for disease of the ankle-joint. Bone very hard, imbedded in soft grey granulations.

A. Organic solids. nitrogenous. 25.358
Fatty — 5.307
30.665.
Salts — 22.556.
Water — 46.558.

B. Organic solids. nitrogenous. 47.646
Fatty — 9.971.
57.617.
Salts — 42.193.

C. nitrogenous solids. 82.7
Fatty substances 17.3.

Analysis 4.

17·012 grammes. Portion of head of femur, removed post mortem from a case of pernicious anaemia. Bone heavy, hard, with dark purplish colour on section. As this bone was left exposed to the air some time before I got it, the amount of water is probably too low.

A. Organic solids. Nitrogenous 22·178.
Fatty — 6·554.
28·732

Salts — 20·632

water — 50·640

B. Organic solids. Nitrogenous 44·927.
Fatty — 13·276
58·203.

Salts — 41·795

C Nitrogenous solids. 77·2.
Fatty substances 22·8.

Analysis 5.

·687 grammes. Syphilitic exfoliation from the frontal bone, spontaneously separated. Bone dry, white, hard, with irregular sharp edges. No diploë separated.

A. Organic solids. Nitrogenous. 38·282.
Fatty --- 1·455
39·737
Salts ---------- 56·477
Water ---------- 3·784

B. Organic solids. Nitrogenous 39·788
Fatty --- 1·512
41·300
Salts ---------- 58·699

C Nitrogenous solids. 96·3
Fatty substances 3·7.

Analysis 6.

6·837 grammes. Slice of lower end of tibia removed in Syme's amputation for disease of the ankle joint in a child. Bone soft, mottled red and yellow. Cartilage quite destroyed.

A. Organic solids. Nitrogenous 17·829
Fatty ——— 12·431
30·260
Salts ——— 9·156.
Water ——— 60·582

B. Organic solids. Nitrogenous 45·235.
Fatty ——— 31·538
76·773
Salts ——— 23·229

C Nitrogenous solids — 59.
Fatty substances — 41.

Analysis 7.

9·864 grammes. Portion of os calcis from same case as no 6. Bone red, brittle, and very spongy. Cartilage strip very easily.

A. Organic solids. Nitrogenous 7·522.
Fatty — 56·733
64·255
Salts — 4·136
Water — 32·116

B. Organic solids. Nitrogenous 10·998
Fatty — 82·952
93·950.
Salts — 6·047

C Nitrogenous solids — 11·7
Fatty substances — 88·3.

Analysis 8.

1.559 grammes. Intrinsic cancer from the same Case as Nos. 6 and 7. Bone soft, friable; mottled red and yellow. Cartilages apparently normal externally, but strip very easily from the bone.

A. Organic solids. Nitrogenous 6.799
Fatty — 63.566
70.365
Salts — 3.842
Water — 25.793

B. Organic solids. Nitrogenous 9.162
Fatty — 85.660
94.822
Salts — 5.177

C. Nitrogenous solids 9.6.
Fatty substances 90.4.

Analysis 9.

5.478 grammes. Portion of incagniatio ex: : quatuma in lower end of femur. Bone hard, white, and dry.

A. Organic solids. nitrogenous. 29.481.
Fatty — 1.989.
31.470
Salts — 42.606.
water — 25.922.

B. Organic solids. nitrogenous 39.798
Fatty — 2.688
42.486
Salts — 57.576

C. nitrogenous solids — 93.67
Fatty substances — 6.33.

Analysis 10.

4·118 grammes. Portion of humerus from an excised elbow-joint in a child. Bone very soft, mottled red and yellow. Cartilage eroded.

A. Organic solids. Nitrogenous. 17·508.
Fatty 24·987
42·495
Salts — — — — — — — — 11·316
Water — — — — — — — — 46·189.

B. Organic solids. Nitrogenous. 32·536
Fatty — — — 46·434
78·970
Salts — — — — — — — — — 21·030

C Nitrogenous solids — 41
Fatty substances — 59.

Analysis 11.

~~3·664~~ 4·055 grammes. Chips from shaft of femur, removed during operation for ununited fracture of some standing (false joint). Presumably healthy.

A. Organic solids. Nitrogenous 36·191.
Fatty ——— 4·192

39·383

Salts ——————————— 55·166

Water ——————————— 5·451?

B. Organic solids. Nitrogenous 37·172.
Fatty ——— 4·433

43·605

Salts ——————————— 57·345.

C. Nitrogenous solids — 89·35
Fatty substances — 10·65.

In this case the bone was exposed for some time to the air so that the proportion of water is too low.

Analysis 12.

8·6 grammes. Portion of lower epiphysis of femur from an amputation for disease of the knee joint. Bones soft, yellow, greasy; Cartilage strips easily. Immediately above the line of the epiphysis the medulla was quite normal in appearance.

A. Organic Solids. Nitrogenous 9.223
Fatty —— 45.553
54.776.
Salts —— 7.964
water —— 37.258.

B. Organic solids. Nitrogenous. 14.700.
Fatty —— 72.517
87.217
Salts —— 12.301

C. Nitrogenous solids — 16.8
Fatty substances — 83.2.

Table 1.

Average per-centage composition of 6 cases (analyses 2, 6, 7, 8, 10 and 12) of the advanced stage of Osteitis.

A.	Organic solids. Nitrogenous.	12·700.	
	Fatty ——	42·570	
		65·270	
	Salts ——		7·730
	Water ——		27·000

B.	Organic solids. Nitrogenous.	22·413	
	Fatty	64·125	
		86·538.	
	Salts ——		13·462.

C	Nitrogenous solids —	27·2
	Fatty substances —	72·8

Table 2.

Average percentage composition of 3 cases of Necrosis. (Analyses 3, 5, and 9).

A	Organic solids. Nitrogenous.	31·040
	Fatty	2·917
		33·957
	Salts	40·526
	Water	25·497.
B.	Organic solids. Nitrogenous.	42·410
	Fatty	4·723
		47·133
	Salts	52·867.
C.	Nitrogenous solids	90·9
	Fatty substances	9·1.

Table 8.

General comparative table of the sections a. of the preceding analyses.

	Organic solids			Salts	Water.
	Nitrogenous	Fatty	Total.		
Normal	36·1	4·1	39·3	55·1	5·4. ?
O. myelitis. early	39·1	11·1	50·3	27·1	22·2
" late	12·7	42·5	65·2	7·7	27·0.
Necrosis	31·0	2·9	38·9	40·5	25·4
Pernic. anaemia	22·1	6·5	28·7	20·6	50·6

Table 4.

General comparative table of the sections B. of the preceding analyses.

	Organic solid			Salts.
	Nitrogenous	Fatty	Total	
Normal	37·1	4·4	43·6	57·3
O. myelitis early	50·4	14·4	64·9	35·0
" late	22·4	64·1	86·5	13·4
Necrosis	42·4	4·7	47·1	52·8
Pernic. anaemia	44·9	13·2	58·2	41·7

General comparative table of the Sections of the preceding analyses.

	Nitrogenous	Fatty.
Normal	89·3	10·6.
O. myelitis - early	73·7	26·3
" late	27·2	72·8
Necrosis	90·9	9·1
Pernic. anaemia	77·2	22·8.

The most notable fact brought out by these tables is the great variation in the proportion of fatty matter to the nitrogenous substances. In cancellous bone, as all the cases of osteomyelitis were, it is natural to expect that the amount of fat in the medulla would be considerable, but the proportion of 73 to 26 indicated in the tables on p. 16 (in one case — analysis 8, p. 11 it was actually 90 to 10) is far beyond the range of normal composition. Even in the early stage of osteo-myelitis, of which analysis 1, p. 4 is an example, the proportion is 26 to 73, in a bone of which the naked eye appearances would not lead to suspicion of fatty degeneration. In the advanced cases of degeneration of the organic tissue the condition indicated by these results must necessarily interfere very decidedly with

the blood supply of the bone and lead almost-
invariable to death of the tissue. The history
of the pathological process must be briefly
somewhat of this nature: inflammatory exud-
ation in the stage of determination and
congestion is probably rapid owing to the
loosely packed structure of the medullary tissue
and the thinness of the walls of the vessels
known to obtain in that tissue. The
forcing of the inflammatory products - serum
and leucocytes - into this loose tissue, which
is, however, packed within the meshes of the
hard, unyielding bony framework, gradually
compresses the blood vessels and so favours
the occurrence of degenerative changes by
materially diminishing the blood supply,
which again is still further interfered with
by the increased bulk of the fatty matter as

compared with the normal tissue which it replaces. Thus it will be seen that the cutting off of the blood supply, though eventually pretty complete, is a gradual process, so that the bone, being slowly starved to death, dies piecemeal or undergoes molecular disintegration (caries). In some cases, undoubtedly, when owing to anatomical peculiarity or other circumstances the blood supply is more rapidly cut off, necrosis ensues, as is occasionally seen in the os calcis and other spongy bones, but in most cases the process is as described above. The condition of the cartilages noticed in the advanced stage of osteomyelitis is accounted for in the same way. The articular cartilages receive their blood

supply from the underlying bone, and this nourishment is gradually cut off in the same way as that of the bone tissue, the result also being the same, namely, fatty degeneration followed by complete disintegration and removal ("ulceration of cartilage" in one of its forms). The intimate union between the cartilage and the articular ends of the bones is destroyed in the same way, and the cartilages are found more or less separated or separable from the bone as noted in the cases described.

In cases of necrosis fatty degeneration does not seem to occur for the highest proportion of fatty to nitrogenous organic substances noted is 17 to 83 (analysis 3, p. 6), the lowest 4 to 96 (analysis 5, p. 8), the

average being 9 to 91 (Table 2, p. 17.), decidedly lower than in the supposed normal case (analysis 11, p 14) where it is 11 to 89, or in the case of Pernicious Anaemia (anal. 4. p. 7) where it is 23 to 77. The small amount of fat found in necrosed bone is most strikingly shown by comparison of analysis No $\frac{14}{12}$, healthy shaft of femur, with No. 13, necrosis of the same bone; in the healthy bone fatty matter constitutes 10 per Cent. by weight of the organic tissue, while in the case of necrosis it only amounts to 6 per cent. It is evident that the mode of death of the bone in necrosis must be quite different from that described as occurring in caries. Owing to the dense structure of the bone in which necrosis is

the rule, a very much smaller amount of inflammatory exudation suffices to completely choke the blood vessels, and death thus being sudden, or at least rapid, fatty degeneration occurs only to a slight extent if at all. The diseased portion of bone thus bears exactly the same relationship to the nutritive processes in the surrounding parts as a superficial slough does. As soon as granulations are formed around it they appear to a certain extent to absorb the disintegrating organic tissue, and, as usual, remove the fatty or oily parts first. This is probably the reason for the very small amount of fatty matter found in such cases as Analysis 5, p. 8, where the proportion of fat to nitrogenous substances is only 4 to 96.

These results are not without important clinical bearing, especially in connection with operations on diseased joints.

In many cases of advanced disease of joints, especially in those termed Strumous, the condition of the bone in the neighbourhood of the joint is as important a consideration, if not more so, as the true state of the soft tissues in the articulations, for it is mainly upon the state of the bones that the success of an operation for partial or complete excision of the joint depends. The complete removal of the diseased soft tissues is a comparatively simple affair, and with antiseptic treatment is a very successful operation, but when diseased bone has to be removed the progress of the case to recovery is seldom so speedy and in many cases healing of the wound is only attained after

subsequent operation for removal of carious portions from the ends of the bones. This is due, of course, to the fact that part of the bone left has been in a stage of disease too far advanced for recovery. Bone obviously carious or necrosed is of course always removed in an operation for excision of a joint, but a bone in a stage of osteo-myelitis far short of this is very apt to be left alone, and subsequently eventuate in carious, necessitating reaction. It is easy to understand that if the sound surface of the bone is very unhealthy the necessary materials for repair will not be supplied, but it is sometimes very difficult to determine at the time of operation whether bone which is certainly nothing like carious is still in such a condition as inevitably to prevent a favourable result.

In some cases, even of pulpy degeneration, where the condition has been primarily one of synovitis and the disease is not of very old standing, the bones and cartilages may be quite normal; but in cases where the degeneration is of the "Scrofulous" character, with greasy pus and masses of curdy material, the bone is invariably more or less diseased. The osteo-myelitis may be in various stages; there may be simple hypervascularity of the bone, the bony tissue being normally firm and resistant, but unnaturally red and juicy looking on section. In such cases the cartilages are found white and glistening, and still firmly adherent to the bone. In other cases a slightly more advanced stage

former hypervascularity or congestion may be found, when the cartilages are still firm, and the section of bone is mottled red and yellow, oozing bloody serum with perhaps a few oil drops on pressure; while in more advanced cases than these the section of bone is quite yellow in colour, the cancellous tissue cuts like cheese, is much ravined, and when it is squeezed almost pure oil may flow out. In these latter cases the cartilage has usually a distinctly yellow tinge, always separates easily from the bone, and may in some spots be eroded or perforated, with the yellow fatty bone appearing through it. In the most advanced cases of "fungous caries", the

bone is carious in spots, the cartilages are more or less completely destroyed, and the ends of the bones on each side of the joint may only be separated by gravelly pus and soft pulpy "granulations" - in reality inflammatory exudation of too indifferent a type to be dignified with the name "granulation".

In the stage of more hypervascularity of the bone when the cartilages are healthy malevergens wound either not touch the bone or at all events not remove more than would be necessary to ensure either proper freedom of movement in certain cases, or proper apposition of the ends of the bones where fixture was desired; and in such cases healthy granulations would speedily form and the case go on to a successful result.

In the most advanced stage of disease again, all the diseased bone would be removed by the saw, forceps, or gouge, till sound bone was reached, or possibly amputation would be unhesitatingly performed.

But it is the intermediate class of cases that give rise to the difficulties above indicated. The condition may be apparently not far removed from normal and the surgeon may be tempted to remove but little of the bone, either in order to avoid amputation or merely on the general principle of sacrificing no more than is absolutely necessary, the ultimate result, however, being that after a time caries is found to have become

established, and the decision to that extent fails. In such cases the results of the investigations of which these analyses and tables are the out-come should furnish an aid to decision. It was found that in all cases, without exception, when the cartilage was in the slightest degree yellow and easily stripped from the bone fatty degeneration of the medulla (advanced osteo-myelitis) was well established, in fact so far advanced as to render recovery of the bone scarcely possible, and it was also found that in all cases this condition existed as far as the line of the epiphysial cartilage at least. The tearing of

this last fact, of course is that if the state of the cartilage noted above is found, the whole epiphysis must be removed.

But this condition of advanced fatty degeneration in many cases extends beyond the epiphysial line or cartilage into the medullary cavity of the shaft, and to remove the whole of the bone as far as this condition extend, would probably in most cases end in immediate amputation. It is fortunately not necessary to remove the whole thickness of the shaft, for if the diseased cancellous bone at the end of the shaft is gouged or scooped out even to a very considerable extent, leaving a shell of firm shaft, the cavity thus formed

with fills up with granulations and heal well. The reason for this is not difficult to find. In the case of the epiphyseis recovery of the bone is prevented by the fact that the blood supply is almost entirely cut off by the advanced stage of degeneration, while in the shaft, on the other hand, the shell which remains after scooping out at the end receives abundant blood supply from the peri: osteum and so is enabled to set up effective reparative processes.

The various points discussed, viz. the unsuccessful results of attempts to save bone, the frequent limitation of the degen: erative changes to the medullary tissues

to the epiphysis, and the good results ob-
tained by scooping out the diseased
tissue from the end of the shaft, are
points which hospital observation is
continually demonstrating, and did time
permit I could give notes of numerous
cases from the journals of the Western
Infirmary where they are well shown.

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