rebuked her, and she cried. She came back the following week and in subsequent weeks, receiving five to ten minutes' chat and a bottle of medicine on each occasion.

"Since then, owing to a greater awareness of personality disorders on my part, she has been given a one-hour interview in which, *inter alia*, she told of her childhood, of a father who was in the Navy and away from home most of the time, of a much-loved younger brother who died at the time of the onset of her symptoms, of her dyspareunia since the beginning of her marriage, and her complete inability to have sexual intercourse since her brother's death. Further investigations are in progress. Her attitude to me since that interview has much changed; there are no more efforts to flirt and there is an improvement in her symptoms. But it took four years to get that hour, and an appendectomy. *Mea culpa!*"

Case 2

The doctor in charge of this case is a well-experienced and rather cautious general practitioner. Although he seemed to be sincerely interested in his patients' psychological problems he was careful, until coming to the course, not to get too much involved with them. He attended for three terms, hardly missed a conference, and, although following the discussions with great interest, even to quoting his own experiences, never tried any real psychotherapy with his patients. Then suddenly he decided to start with one case, and on the same day the case of which the following is his report occurred in his practice. It was this case which he started reporting with the phrase, "I did a real Smith—and it worked."

"The patient, a boiler coverer, aged 26, was a quiet, thin, pale, neat, inoffensive young fellow. Married three weeks before. Severe headaches. No relief in tab. codein. Pain 'behind eyes'; feels 'something wrong with brain.' Cannot go to sleep, and wife has to sit with him and hold his hand. Worries about 'floods.' For the last two months he could not go to the cinema; he gets lost in the film and suddenly 'comes to,' gets a 'crowded-in feeling,' feels panicky, screen seems to recede, and he has to rush out of the cinema. He also fears boilers now and is jumpy when working on them. He has always found it hard to make friends and is content to be by himself.

"No sex life before marriage. Satisfactory now for him, but wife has to be manually masturbated to achieve orgasm. ('I feel funny telling you that.') Feels content sitting in in-laws' house now, in spite of noise of numerous children, but is not so happy about going out. His wife has recently recovered from pulmonary tuberculosis and is at work again. The patient is very 'fussy'; does all the housework himself because he likes to do it, not of necessity. Gets a 'kick' out of giving his wife breakfast in bed.

"*Family History.*—Mother died when he was 3 years old, and he and his two elder brothers were sent to an orphanage, where he stayed until 14. Father had tabes and was blind. When the patient left the orphanage he became the maid-of-all-work at home. It was he who did the shopping and cooking and cleaning. He led his father about all the time, not his brothers. (This I remember very well, as I used to treat his father and knew the family set-up well.) His only hobby was motor-cycling, and he always took his father out on the motor-cycle. He thinks his father's blindness was due to war injuries and experiences. He himself often wondered what it was like to be blind, and often did a 'silly thing'—drove his motor-cycle blind to see what it felt like. His father's mother was blind (he was told) and she was also the youngest in her family.

"He dislikes his elder brother intensely and the dislike is reciprocated. This brother always acted the big boss: he expected to be waited on, 'took everything for granted,' and expected the patient to wait on him like a slave. The brother does not drink nor smoke, and is a highly critical sort of chap. He even supervised the patient's courtship, told him when he should get home at night, and strongly advised him against marriage. The brother's marriage broke up after three weeks and was 'annulled' (that was the word he had heard used.) The patient was afraid of him, but now they are not on speaking terms and pass each other in the street.

"Two weeks ago the patient was admitted to hospital for investigation because of the severity of the headaches: He was discharged after a few days, being told it was his 'nerves.'

"*Hospital Notes* (seen by me).—'Came to hospital in taxi as he could not walk owing to severity of headaches. Admitted: ? sinusitis; ? migraine. Investigated, and no organic cause found. C.N.S. clear. Discharged. To be seen again next week. ? Psychiatrist.'

"March 13, 1953.—He reported to me immediately after he left hospital, complaining that headaches were still persistent and

that he could not get to sleep. 'I don't know why I should be like this; after all, it is the first time in my life I have been free from financial worry—for example, paying off motor-cycle—and wife is over her T.B. and is working. Thus I can have little luxuries I could not afford before.'

"*Immediate Interpretation After Taking History.**—Assured not organic and nothing to do with father's blindness. 'You have always been pushed around since childhood and always in an inferior position. The Cinderella of the family. You had no right to be all right. You always had to carry a burden and had no right to affection (which you really craved). Now you are suddenly free of your tasks (through which you were playing out your inferior position) and you are immediately obsessed with guilt. So you have to atone with a symptom—the obvious one being headache—behind eyes—associating yourself with your father, to whom you were attached (and perhaps unconsciously resented).' 'I thought of that myself.'

"March 16.—Saw the patient again. He said he felt 'marvellous.' No headaches; knows it is not organic now and understands symptoms are due to his previous life; sleeps through the night and goes off to sleep immediately; not frightened in a crowd, and is very grateful.

"May 7.—The patient has been back at work since March, is very happy with his wife, sleeps well, and has no complaints at all."

Postscript when reading the proofs.—Report of the practitioner on October 22: "Man not seen for several months, only wife, who reported that he was fine. He occasionally gets headaches, which do not amount to anything, and he continues working. He is much easier to live with, and from the point of view of the wife he is a complete cure."

MYELOMATA OF BONE A REVIEW OF 25 CASES

BY

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Myelomata are said to be the rarest form of bone tumour (Geschickter and Copeland, 1936; Cade *et al.* 1947), yet of 25 cases here reported 24 have been treated in this hospital group over the past five years, and one of us (A. N.) has had nine under his care in the past two years. During this same five-year period 13 cases of osteogenic sarcomata of bone (including three cases arising in Paget's disease) have been treated in the Bradford Regional Radium Institute. Osteogenic sarcoma is given considerable prominence in medical textbooks, yet it is apparent that its incidence is less than that of myelomata of bone. We suspect the incidence of the latter is not so uncommon as is usually suggested, and believe that many cases are wrongly diagnosed as secondary carcinomata or never diagnosed. Four cases in this series were diagnosed only when the patient was admitted *in extremis*. One is apt to associate myelomata with the textbook picture of multiple discrete osteolytic lesions in the skull, clavicle, vertebrae, and ribs, but this is usually the terminal picture. Hence one finds that most cases have a history lasting one to two years before the diagnosis is made. Early diagnosis is difficult because the condition is often asymptomatic for a long period, while signs and bio-

*This interpretation was what the doctor described as: "I did a real Smith."

chemical changes are very variable and not all are present in an established case. We wish to emphasize that one or more negative investigations do not exclude the condition, and the whole gamut of confirmatory tests is required before we can be confident of its absence.

While textbook descriptions stress the multiplicity of the lesions, and this is no doubt the commonest type, solitary and diffuse forms of the condition are encountered. The tumours are soft, reddish purple in colour, and vascular, although central necrosis may be present in large tumours (Case 4). They consist of ovoid or pyriform cells with a nucleus which has a nucleolus and a typical "clock" or cartwheel appearance due to dense chromatin.

We find the disease to exist in three forms: (1) a solitary form in which a large tumour is present; (2) a diffuse form in which the lesions are small and cause a diffuse decalcification of the affected bone; and (3) a multiple form into which the others usually develop when the plasma cells are aggregated into discrete nodules forming localized osteolytic lesions.

Myelomata Initially Solitary

Willis (1941) enunciated the criteria which determine the diagnosis of solitary myeloma—histological diagnosis, radiographs of the entire skeleton at regular intervals, and the absence of Bence Jones proteose from the urine. Only 23 cases of proved solitary myeloma have been described (Lumb, 1952). Many described as such have subsequently become multiple. The solitary tumours are large and affect the long bones and spine (Chesterman, 1935; Willis, 1941) as opposed to the affection of the flat bones and ribs by the multiple form.

There is little doubt that many myelomata are solitary initially, but the picture of multiple myelomata usually develops. It is therefore probable that this form and those which appear to be initially multiple are a single pathological entity, the rate of metastasis being extremely rapid in the multiple form, which is the end-stage of the disease. Some pathologists, however, maintain that multiple myelomatosis is a multifocal systemic disease without metastasis (Lumb and Prosser, 1938) and that the solitary myeloma is a separate entity. This view is difficult to reconcile with our experience and the other recorded cases of solitary tumours which ultimately disseminate (Cutler, Busch, and Cantril, 1936).

Case 1.—In November, 1944, a man aged 36 fell on to his sacrum. In July, 1945, he developed severe pain in the lumbo-sacral region and both legs. X-ray examination revealed the presence of a multilocular cystic tumour involving the entire sacrum. The sacrum was expanded and the cortex eroded anteriorly. Trabeculation was present. Biopsy on July 21 showed typical plasmacytoma. The blood picture was normal. Deep x-ray therapy was given. He remained well and there were no deposits in the ribs until July, 1951. Sternal puncture then showed myelomatosis to be present. In August he was given a course of stilbamidine and deep x-ray therapy, which relieved his pain a little. The patient is still alive, but is confined to bed owing to his rapidly deteriorating condition. *Comment:* This tumour remained solitary for seven years, but ultimately the typical multiple form developed.

Case 2.—A woman aged 63 was first seen in 1947. She complained of pain in the right loin for two years and had

recently noticed a lump in this situation. An x-ray film showed rarefaction of the twelfth rib. Kahn test negative. Tumour excised—section showed a tumour of undifferentiated round cells and no definite pathological diagnosis made. Two years later she had a similar mass over the left sixth rib. Bence Jones protein absent from urine. Mass excised but no definite pathological diagnosis made. On March 30, 1950, a further mass was removed from a rib which proved on section to be a myeloma. The patient died one year later.

Case 3.—In May, 1948, a man aged 41 fell from a ladder and attended hospital. X-ray film revealed solitary cyst in the upper end of the femur. The other long bones, ribs, and skull were not examined radiologically. Biopsy revealed the presence of a plasmocytoma. Deep x-ray therapy was given. In August he was readmitted and died within twelve days. X-ray examination revealed punctate osteolyte lesions in ribs, skull, and pelvis. Urine: Bence Jones protein and albumin present. Blood: Hb, 55%; W.B.C., 6,000; moderate rouleaux formation; total protein, 12.8 g.% (albumin 3.0 g., globulin 9.8 g.); A/G ratio, 1:3.27. Necropsy confirmed the diagnosis of multiple myeloma.

Case 4.—This case represents the closest approach to the solitary plasmocytoma in this series. The patient, a man aged 28, was seen on February 21, 1952. The first symptom was pain below the knee, present for the previous nine weeks. It was worse when he walked. Examination revealed tenderness over the tibial condyle, no effusion in knee, and full knee movements. An x-ray film showed a

FIGS. 1 and 2.—Case 4. Myeloma of tibia.

multilocular cyst in the upper end of the tibia extending down the shaft, but not expanding the cortex. On later review two small translucent areas could be seen below the main cyst (Figs. 1 and 2). Films of the skull, ribs, and long bones showed no other tumour. Urine: Bence Jones protein absent. Biopsy: typical plasmocytoma—central necrosis of the tumour present at operation; Unna-Pappenheim staining showed typical plasma cells. Sternal puncture, normal. Blood: acid phosphatase, 1.3 units; alkaline phosphatase, 4.3 units; total plasma protein, 6.8 g.% (albumin 3.8 g., globulin 2.8 g.); A/G ratio, 1.5:1. An x-ray film four weeks later showed two small translucent areas in the skull. Deep x-ray therapy was given. The symptoms cleared and he walked without pain or limp. The tumour has not enlarged and no further changes have occurred in other bones. Plasma protein is still unchanged. *Comment:* This case would appear to resemble that described by Chesterman, but the two nodules in the skull suggest that multiple lesions will appear at some future date.

In the cases described above, Bence Jones protein was absent in two, and present in one when multiple lesions had appeared. It is probable that changes in plasma globulin and A/G ratio are late changes and present only when there are multiple deposits.

Multiple Myeloma

The established multiple myelomatosis may appear in circumscribed or diffuse forms, and again the latter may develop into the former. The picture of the circumscribed variety is that which we have been apt to assume from our textbooks as the only type, but the well-established picture of multiple osteolytic lesions in the skull, pelvis, scapulae, ribs, and other bones appears to be a late stage in the disease. Unfortunately diagnosis before this stage is reached is not always possible, as many diagnostic features may be absent; and, as there is often a paucity of symptoms, or none, its presence is often unsuspected. The presenting symptoms are variable, but localized pain, especially persistent backache, was a feature in many, and paraplegia was present in two of our cases. It is possible that the discrete punctate form is preceded by a diffuse form producing general decalcification. Then discrete nodules produce osteolytic areas.

Case 5.—Man aged 56. Presenting symptoms and signs: ascites and ulceration of mouth. Diagnosis: cardiac failure and thrombosis. Ultimately diagnosed as multiple myeloma. Died without treatment. Blood picture: Hb, 47%; E.S.R., 83 mm.; W.B.C., 8,600; marked rouleaux formation present. Sternal puncture, plasma-cell myelomatosis. Blood urea, 40 mg. per 100 ml. Total protein, 11.5 g.% (albumin 1.9 g., globulin 9.6 g.); A/G ratio 1:5. X-ray films showed multiple punctate osteolytic areas in skull, ribs, and pelvis. Urine: Bence Jones protein absent.

Case 6.—Man aged 42. Presenting symptoms: proptosis and headaches. X-ray films revealed multiple punctate areas of erosion in the skull. No changes in ribs and other bones. Blood protein and A/G ratio unchanged initially, but after two months the total protein was raised and the A/G ratio became 1:3.8. Course of stilbamidine given. Died four months later. *Note:* Normal proteins initially.

Case 7.—Woman aged 64. Presenting symptoms: lassitude and dyspnoea for six weeks. Died within two weeks of attendance at hospital. Sternal puncture positive for myeloma. X-ray films showed punctate areas in ribs and skull. Plasma-protein estimations and presence or absence of Bence Jones protein not recorded.

Case 8.—Woman aged 58. Presenting symptoms: nausea and cough for six weeks. Died two weeks after hospital admission. X-ray films showed multiple punctate areas of erosion in ribs, skull, and pelvis. Blood picture: Hb, 80%; W.B.C., 10,000; urea, 120 mg. per 100 ml.; protein not estimated.

Case 9.—A man aged 53 had backache for four months and then developed weakness and paraesthesia in one leg after three months. Paraplegia developed and he was admitted. Examination showed paraplegia due to lesions at level of D8. X-ray films showed osteolytic lesions in ribs and skull, with compression of D7 vertebral body. Disk spaces intact. Blood: protein 7.4 g.%, A/G ratio normal; acid phosphatase 1.5 units. Urine: Bence Jones protein absent. Deep x-ray therapy and stilbamidine given. Readmitted eight months later; no change in paraplegia; deposits in shoulder girdle and cervical spine. Died 13 months after first attendance.

Case 10.—Man aged 58. December 8, 1950:—presenting symptoms: cough for six weeks and tumour of angle of mandible extending to ramus. X-ray film showed obstruction of angle of mandible with erosion of ramus. December 14:—biopsy: typical plasma-cell myeloma. January 15, 1951: x-ray film showed erosion of first rib. February: course of deep x-ray therapy given—3,000 r to mandible and shoulders. May 9: x-ray films showed defect in upper end of femur; no destructive lesion in spine. Incontinence

of urine. Suprapubic cystotomy performed. Test for Bence Jones protein not performed. Further deep x-ray therapy and nitrogen mustard given without effect. Patient died on July 27, 1952.

Case 11.—Woman aged 64, referred from radiotherapy department May, 1949, with ? osteoclastoma of sternum. Presenting symptoms: backache, pain in chest and arms for six months. X-ray film showed loculated tumour in manubrium sterni. No other radiographs of bones taken. Deep x-ray therapy given. In November, 1949, pain had been relieved but tumour unchanged. X-ray examination showed translucent areas in several ribs and right clavicle. Urine: Bence Jones proteose present. E.S.R. 47 mm. Total plasma protein, 6.6 g.% (albumin 2.9 g., fibrinogen 0.17 g., globulin 2.9 g.); A/G ratio 1:1. Course of nitrogen mustard therapy given in January, 1950. In July, 1950, x-ray examination showed no further changes. Patient died September, 1951; own doctor stated cause to be "coronary thrombosis due to hyperpiesis."

Case 12.—Man aged 68. Presenting symptoms: breathlessness, diplopia, and numbness of face for three weeks. X-ray film of skull showed punctate areas typical of myelomatosis. No lesion in pelvis. Total protein, 7.5 g.% (albumin 5.7 g., globulin 1.8 g.); A/G ratio, 3.1:1. Alkaline phosphatase, 4.4 units; acid phosphatase, 0.9 unit; blood urea, 210 mg. per 100 ml.; E.S.R., 13 mm.; W.B.C., 12,000; Hb, 90%. Urine: Bence Jones proteose absent. Sternal puncture: typical of myelomatosis. Died two weeks after initial observation.

Case 13.—Woman aged 47. Presenting symptoms: feeling of weakness for many years, backache for six months, exophthalmos. Blood: cholesterol, 250 mg. per 100 ml.; total protein 7.9 g.% (albumin 6.2 g., globulin 1.7 g.); A/G ratio, 3.6:1; Hb, 90%. Sternal puncture: normal. Urine: Bence Jones proteose absent. X-ray film of skull: punctate areas typical of myelomatosis; no lesion in other bones.

Case 14.—Woman aged 64. May 12, 1952:—presenting symptoms: pain in right lower ribs. Blood: Hb, 48%; R.B.C., 2,900,000; W.B.C., 4,400; total protein, 11.0 g.% (albumin 5.1 g., globulin 5.5 g.); A/G ratio, 1:1. Urine: Bence Jones proteose present. X-ray films showed multiple destructive lesions in ribs and skull, with generalized decalcification. Stilbamidine and deep x-ray therapy given. Last seen July 30, 1953. Pain then considerably relieved.

Case 15.—Man aged 71. July 30, 1952:—presenting symptoms: repeated epistaxis and melaena. X-ray films showed multiple small areas of translucence in skull, right humerus, and right femur. Blood: total protein, 7.95 g.% (albumin 2.65 g., globulin 5.3 g.); A/G ratio, 1:2. Course of deep x-ray therapy given.

Case 16.—Woman aged 59. Presenting symptoms: low back pain for eighteen months, unrelieved by bed rest or plaster immobilization. X-ray films showed general decalcification of lumbar and dorsal spine and pelvis. Blood: total proteins, 8.0 g.% (albumin 3.9 g., globulin 3.8 g.); A/G ratio, 1:1; calcium, 10 mg. per 100 ml.; phosphorus, 3.2 mg. per 100 ml.; Hb, 68%; W.B.C., 9,000. Some months later x-ray films showed typical punctate areas in ribs, pelvis, and skull. Sternal puncture: typical myelomatosis. Urine: Bence Jones proteose absent. Deep x-ray therapy relieved pain. Died three months after treatment. *Comment:* This case demonstrates the diffuse decalcification, followed by the appearance of the typical multiple osteolytic lesions.

Case 17.—Woman aged 60, seen in 1950. Presenting symptoms: pain in dorsal region for about three months. Had kyphosis and tenderness at D9-10. X-ray films showed collapse of D9; no lesions in ribs. Thought to have secondary carcinoma, but no primary lesion found. Six months later x-ray examination showed no further radiological changes; no lesions in ribs or humerus. Twelve months later, x-ray films showed punctate areas in dorsal and lumbar spine, skull, and long bones. Sternal puncture: typical myelomatosis. Urine: Bence Jones proteose

present. Blood: total protein, 6.0 g.% (albumin 5.2 g., globulin 0.8 g.); A/G ratio 6.5 : 1. The patient is still alive. Has had a course of stilbamidine without demonstrable effect. No deep x-ray therapy given. Note normal serum proteins when all other typical changes were present.

Case 18.—Woman aged 56. Admitted February 18, 1953, with fractured shaft of right femur. There had been pain in the knee for the two previous months. X-ray films showed a fracture through a large cyst at junction of lower and middle thirds of femur. X-ray films of ribs, clavicle, scapula, and skull showed multiple osteolytic areas with no new bone formation. Uroselectan showed normal renal function. Urine: no Bence Jones proteose present on repeated testing. Blood: W.R. negative; blood urea, 27 mg. per 100 ml.; total protein, 5.7 g.% (albumin 2.97 g., globulin 2.4 g.); A/G ratio, 1.2 : 1 (same when repeated after three weeks). E.S.R., 45 mm. per hour. R.B.C., 3,800,000; W.B.C., 10,000; Hb, 69%. Sternal puncture: positive for myelomatosis. Biopsy of nodule in left acromion process showed plasma-cell myeloma.

Case 19.—Woman aged 66. Admitted with history of increasing shortness of breath and weakness for a year. Doctor had noted that she was anaemic six months previously, and started some liver injections with no improvement. Three months previously she developed severe back-ache, which was aggravated by any attempt at movement, and was admitted in this condition. Had vague aching in most joints. No marked physical features. Bence Jones proteose—positive. Total serum protein, 7.2 g.% (albumin 3.4 g., globulin 3.8 g.); A/G ratio, 1 : 1.1. Blood urea, 40 mg. per 100 ml. X-ray film showed no change in skull. Some compression of D 5, 6, and 7, with decalcification. Generalized osteoporosis of dorsal and lumbar spine. Osteolytic areas in ribs and sternum. Sternal marrow puncture: 90% of cells were plasma cells. Blood count: Hb, 22%; leucocytes, 3,800.

Case 20.—Woman aged 69. Presenting symptoms: shortness of breath and feeling of tiredness for six months. Physical examination showed no definite features. X-ray films of skull, femora, and pelvis showed bone detail within normal limits. Old fracture of right clavicle and left eighth rib. Area of rarefaction in left clavicle. Sternal puncture: numerous lymphoid cells and abnormal early cells; ? localized deposit of leukaemia. Bence Jones proteose—negative; trace of albumin in urine. Blood: total plasma protein, 9.3 g.% (albumin 1.3 g., globulin 7.7 g.); A/G ratio, 1 : 5.9; Hb, 48%; leucocytes, 7,300 (lymphocytes 2,701; polymorphs 2,236; myelocytes, 1,633). The patient died two months after admission. Necropsy: skull normal; sternum filled with whitish nodules; vertebrae contained similar white areas of marrow in lumbar region and upper end of femur. Sections taken showed myeloma, although cells resemble lymphocytes.

Case 21.—Woman aged 56. Presenting signs: pain in neck, radiating into occiput and to left shoulder and left clavicle. Developed stiff shoulder, which was treated and which has improved; but she still has some pain in the neck. Has noticed prominence of inner end of clavicle. X-ray film showed soap-bubble rarefaction of inner end of clavicle. Biopsy showed myeloma cells. Sternal puncture: myelomata; many atypical plasma cells. Bence Jones proteose—negative; trace of albumin in urine. Blood: total plasma protein, 10.1 g.% (albumin 3.1 g., globulin 6.58 g.); A/G ratio, 1 : 2.1. X-ray film shows small area of rarefaction in the ribs. Skull: one area of rarefaction. Femur and lumbar spine: N.A.D. Dorsal spine: no areas of destruction.

Diffuse Type

Case 22.—Woman aged 66. Presenting symptoms: pain in dorsal and lumbar regions for two years; increasing kyphosis for past six months; poor general condition, with

marked kyphosis. X-ray films showed general decalcification of dorsal spine. No destructive lesion in ribs or spine. Sternal puncture: positive for myelomatosis. Patient developed paraplegia within one month of examination and died.

Case 23.—Woman aged 68. Presenting symptoms: (1) dorsal pain for eighteen months, x-ray film one year previously showing osteoarthritic change, for which physiotherapy gave some relief; (2) increasing kyphosis over the past six months. X-ray films showed general decalcification and collapse of all dorsal vertebrae. No other destructive lesion in spine or ribs. Blood: total protein, 10.3 g.% (albumin 3.8 g., globulin 5.88 g.); A/G ratio, 1 : 1.5; Hb, 48%; W.B.C., 3,000; calcium, 10.5 mg. per 100 ml.; phosphorus, 4.8 mg. per 100 ml.; alkaline phosphatase, 4.6 units. Sternal puncture: typical of myelomatosis. Urine: Bence Jones proteose absent initially, but present three weeks later. Stilbamidine therapy given. Died within two months of conclusion of course.

Case 24.—Woman aged 72. Presenting symptoms: exhaustion for two years; low back pain for nine months. X-ray film showed diffuse decalcification of dorsal and lumbar spine with collapse of D 12. Disk spaces intact. Ribs decalcified, but no destructive lesion. Three months later, x-ray examination showed further collapse of D 12 and fractures of ribs, but no changes in skull. Sternal puncture: typical myelomatosis picture. Blood: Hb, 55%; W.B.C., 4,000; blood urea, 72 mg. per 100 ml.; total protein, 12 g.% (albumin 3.8 g., globulin 8.2 g.); A/G ratio, 1 : 2.36; E.S.R., 67 mm.; serum calcium, 13.8 mg. per 100 ml.; phosphorus, 3.5 mg. per 100 ml.; alkaline phosphatase, 10.4 units. Urine: albuminuria present; Bence Jones proteose absent. No treatment given. Diagnosis confirmed at necropsy.

Case 25.—Man aged 67. Presenting symptoms: low back pain for six weeks. Nothing abnormal on examination. X-ray film showed collapse of D 11; chest and ribs, N.A.D. Blood: Hb, 83%; W.B.C., 4,100; E.S.R., 55 mm.; total protein, 7.8 g.%; A/G ratio normal. Thought to be secondary carcinoma, but no primary neoplasm discovered. Deep x-ray therapy given, with relief of pain. X-ray examination two months later showed no further changes. Four months later patient developed severe pain and anaemia. Blood: Hb, 51%; W.B.C., 4,600; total protein, 10.6 g.% (albumin 2.1 g., globulin 6.5 g.); A/G ratio, 1 : 3. X-ray films showed general demineralization of spine and ribs, but further collapse of D 11, with collapse of L 1 and 2. Sternal puncture: negative. Died two months later. *Comment:* Note the late appearance of serum protein changes.

Discussion

From a study of these cases we see that the large solitary myeloma occurs in the younger age group (average 40 years), but ultimate spread to the multiple form was experienced in all our cases. The diffuse form occurred in subjects over the age of 60 and proved to be the most difficult type to diagnose. The sex ratio in the solitary type was 3 males to 1 female, whilst in the multiple type the female sex predominated (11 females to 7 males). Of the discrete multiple type, two (Cases 16 and 17) were initially diffuse, and discrete punctate lesions developed after an interval, while simultaneous general decalcification was present in Case 14.

Local pain is the most common initial symptom, but pathological fracture and paraplegia are frequent presenting symptoms. The destruction of isolated vertebrae is apt to be confused with secondary carcinoma, and full investigation must be carried out in all cases. This should consist of: radiographic examination of the skull, ribs, and vertebrae; estimation of the total serum proteins and serum albumin and globulin; examination of the urine for Bence Jones proteose; and sternal marrow puncture.

The presence of Bence Jones proteose in the urine is a useful confirmatory test, but is often negative in the multiple cases, and its absence is of no significance in diagnosis. Further, it may be present rarely in other conditions—for example, secondary carcinoma of bone and myelogenous leukaemia.

In our series the test was positive in seven and negative in seven of the cases in which multiple lesions were present. It is negative while a myeloma remains solitary. This approximates to the figures given by Bayrd and Heck (1947), who found the test positive in 53% of the cases.

The serum-protein changes, when present, are diagnostic. There is usually a rise in the total serum protein, due to increase in the globulin fraction, leading to reversal of the albumin/globulin ratio. In the multiple cases in our series these changes were present in 13 and absent in 4, whilst they were not recorded in 4 cases. The change took place at a very late stage in Case 25. A normal serum-protein value does not exclude the diagnosis of myeloma, and the test has no prognostic value.

The blood picture varied extensively, but a severe reduction of the red-cell count was present only in the later stages of the disease in the multiple lesions, while little change in the white-cell count was experienced. A count within or near normal limits may be obtained in the presence of myelomata. A high E.S.R. was often recorded, and this may be associated with the increased serum globulin, as is the phenomenon of the increased rouleaux formation often seen in this disease. Sternal puncture was performed in 14 cases, with a positive diagnosis of myelomatosis in 12 of these.

In reaching a diagnosis we wish to emphasize the need for radiological examination of all bones and completion in all the tests discussed. Biopsy is usually required in the solitary type, as radiological differentiation from osteoclastoma is usually impossible. In lesions of the vertebrae we noted that decalcification followed by compression and destruction occurred, but the intervertebral disks were not affected. In this respect the condition resembles secondary carcinoma and differs from a tuberculous lesion. The frequency of backache as an initial symptom is noteworthy, and the condition should be borne in mind as the cause of such symptoms in the elderly, especially in the presence of osteoporosis and where the pain is unrelieved by rest or immobilization.

Treatment

The results of all forms of treatment make dismal and depressing reading, as these are of no avail in preventing the ultimate death of the patient. One wonders if the patients would not live equally long without treatment. Tennant (1945) described the case of a patient who was still alive five years after diagnosis and who had received no treatment. In our series one was still alive after the appearance of myeloma of the spine two years previously, although a course of stilbamidine had been given recently; while one was still alive seven years after deep x-ray treatment of an initially solitary tumour.

Of those initially solitary, in this series two were given deep x-ray therapy, one being still alive seven years after initial treatment, the other being still alive one year after treatment. One patient died without treatment, and the remaining case did not survive local excision.

It would seem that deep x-ray therapy is of no value in prolonging life in the multiple form, at least when administered when the full clinical picture is present. It is probable that this is the end-stage, and all treatment then will be of no avail. Deep x-ray therapy is of palliative value in relieving localized pain. Eight cases had such therapy alone, and seven survived an average of only nine months, the longest survival being two years. Three had deep x-ray therapy combined with stilbamidine, and died without the treatment having any appreciable effect on the course of the disease.

We have no proof of the value of stilbamidine in the treatment of myelomatosis. Three were treated with stilbamidine alone, and two died within two to four months of treatment. One was still alive six months after therapy. Nitrogen mustard administration also had no therapeutic value.

Consideration of this series of cases suggests that myelomata are not rare, but if the possibility of the presence of the condition is not realized diagnosis is belated. Early and full investigation should be made with this in mind. Full radiological investigation is also of value from the prognostic aspect, as cases in which the myeloma is initially solitary have a longer survival. Successful treatment of malignant disease requires early diagnosis, yet, with myelomata, we have tended to diagnose only the fully established condition. An analogous position would be where diagnosis of carcinoma or sarcoma is made only when metastases are present: when such a condition is reached treatment is of no avail. Hence we can expect little else if we wait until the similar dissemination has occurred with myelomata before we begin treatment.

We believe that the present textbook description of multiple myeloma is that of the end-stage of the disease and that it is analogous to the condition of general carcinomatosis. For efficient treatment we must diagnose the lesion at a much earlier stage. This problem still remains, but if we bear in mind that myeloma is a much more common condition than it was thought to be, we may be able to observe its early manifestations.

Summary

Twenty-five cases of myeloma of bone are reviewed to call attention to their frequency, as it is thought that they are not so rare as one is led to believe.

The difficulty of diagnosis of a disease which is often present in the absence of symptoms is discussed.

Treatment at present available has a questionable effect on the ultimate fate of the patient, but deep x-ray therapy has a definite place in the relief of pain and may prevent the onset of paraplegia when given to affected vertebrae. A case surviving seven years is recorded.

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REFERENCES

- Bayrd, E. D., and Heck, F. J. (1947). *J. Amer. med. Ass.*, **133**, 147.
Cade, S., Scarff, R. W., Golding, F. C., and Adams, S. B. (1947). *Brit. J. Radiol.*, **20**, 10.
Chesterman, J. T. (1935). *Brit. J. Surg.*, **23**, 727.
Cutler, M., Buschke, F., and Cantril, S. T. (1936). *Surg. Obstet. Gynec.*, **62**, 918.
Geschickter, C. F., and Copeland, M. M. (1936). *Tumours of Bone*. New York.
Lumb, G. (1952). *Ann. roy. Coll. Surg. Engl.*, **10**, 241.
— and Prosser, T. M. (1948). *J. Bone Jt Surg.*, **30B**, 124.
Tennant, W. (1945). *Brit. J. Surg.*, **32**, 471.
Willis, R. A. (1941). *J. Path. Bact.*, **53**, 77.

In his annual report for 1952 Dr. W. S. Walton, medical officer of health of Newcastle-upon-Tyne, describes the unsatisfactory housing conditions in that city. Though progress has been made in the building of new houses, "the city has a very long way to go before the living conditions of many of the inhabitants can be brought up to what might be termed ordinary reasonable English health standards of the mid-twentieth century." Out of every 100 households in the city 38 do not possess a separate bath, 18 are without separate water-closet, and 17 have no piped supply of water. About 18,800 of the 87,800 households in the city at the time of the 1951 census lived in one- or in two-roomed "dwellings." The index of persons per room—0.88 in Newcastle—is one of the highest for any area in England and Wales.