

SUGGESTIVE POINTS OF ANALOGY BETWEEN
OTOSCLEROSIS AND ARTHRITIS DEFORMANS.*

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The literature of chronic nonsuppurative diseases of the ear and joints is very extensive, and for the purpose of considering the analogy indicated by the title of this paper, I am putting forward the summary or gist of the views held by many of the best known authorities, and place them under headings which are chosen to emphasize the numerous points or features wherein these diseases seem to have a striking similarity.

It is now the custom for many writers to regard arthritis deformans as a group of diseases, namely, rheumatoid arthritis, osteoarthritis, and spondylitis deformans. As many of the most exhaustive descriptions of chronic nonsuppurative joint affections are given under the title arthritis deformans, I have retained this form of nomenclature. It is, however, a little inconvenient, as it gives a combined picture of certain characteristics, such as the morbid changes, which some writers separate and place under the headings of rheumatoid and osteoarthritis respectively. Painter¹ calls the former atrophic and the latter hypertrophic arthritis.

The chronic nonsuppurative diseases of the ear which should be considered fully, to complete the analogy with arthritis deformans, are otosclerosis and chronic adhesive catarrhal processes, or, as Kerrison² calls the latter, chronic hyperplastic otitis media. As this would necessitate a much more extensive paper than the time at my disposal here permits, I have chosen otosclerosis alone to consider fully, but will refer in my conclusions to the marked analogy which, I submit,

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exists also between chronic adhesive processes and arthritis deformans.

Lucae³ has asserted that it is not possible to separate otosclerosis and adhesive catarrhal processes clinically, but Politzer⁴ differs from this view. Most present day otologists seem to be of the same opinion as Politzer, but many of the fuller descriptions of otosclerosis to be found still unavoidably mix up several of the main features of these two chronic ear affections, as is done in chronic diseases of joints.

The following are the headings under which points of analogy between otosclerosis and arthritis deformans are shown: Definition, etiology, course of disease, symmetry, trophic changes, morbid anatomy, pathogeny, and lines of treatment. Bearing upon etiology, the influence of age, sex, heredity, race, climate and other diseases and conditions, which are said to act as exciting causes of onset or exacerbations, are considered, and finally certain conclusions will be set forth.

DEFINITION.

Otosclerosis.—Poltizer calls otosclerosis a progressive form of deafness, running its course without any catarrhal symptoms and presenting an entirely different character from the adhesive processes secondary to catarrh.

Kerrison gives the following definition: "The term otosclerosis is employed to describe the condition in which, independently of the health or intercurrent disease of the tympanum, the bony capsule surrounding the labyrinth is the seat of chronic nonsuppurative disease interfering with the function of hearing."

Arthritis Deformans.—Osler⁵ describes it as a chronic disease of joints, characterized by changes in the synovial membranes and periarticular tissues, and in some cases by atrophic and hypertrophic changes in bones.

Keen⁶ refers to it as a progressive nonsuppurative disease of joints, manifested by pain, swelling and impaired function, and leading to stiffness and deformity.

Llewellyn-Jones,⁷ describing osteoarthritis, says it is a chronic oligoarticular disease of joints, the widely distributed form of which is most common in women, insidious in onset, running a slow, progressive course, the subjects of the disease being usually well nourished.

AGE.

Otosclerosis.—Gray⁸ says that it is most frequent in middle life, rare under twenty, the majority of cases occurring between twenty and forty.

The commonest age incidence, according to Milligan,⁹ is between fifteen and thirty.

Politzer states that it occurs especially often in elderly people, often in young healthy individuals, but those with a hereditary taint have symptoms marked at ten to fifteen.

Lake¹⁰ gives the greatest incidence as occurring in young adult life, and states that it may begin even in childhood.

Arthritis Deformans.—The majority of Osler and McCrae's cases occurred between twenty and forty approximately. Half their cases began before the age of thirty years.

Llewellyn-Jones gives twenty to thirty as the period of greatest age incidence for rheumatoid arthritis, and says that osteoarthritis is commonest in middle and late life, but occurs in young females and even in children.

The majority of Garrod's¹¹ cases of arthritis deformans occurred between twenty and forty.

Painter says that rheumatoid arthritis is a disease of youth and middle life, and osteoarthritis of middle and late adult life.

SEX.

Otosclerosis.—Gray, quoting Bezold and Denker's combined cases, gives 60 per cent as occurring in women. Pierce¹² gives 60 per cent also, but Yearsley's¹³ cases were as high as 83 per cent in females.

Politzer, Lake and Milligan state that females are more commonly affected than males.

Arthritis Deformans.—Painter says that osteoarthritis is more common in women than in men, but is more crippling in men, as the smaller joints are affected in women.

In Garrod's 500 cases of arthritis deformans, women were affected in 82 per cent.

In Llewellyn-Jones' 240 cases of rheumatoid arthritis, 83 per cent occurred in women. He also states that osteoarthritis is more common in females than in males.

Osler and McCrae, as well as Stewart,¹⁴ give 50 per cent as the incidence in women.

HEREDITY.

Otosclerosis.—Bezold¹⁵ found a history of heredity in 52, Denker¹⁶ in 40.5, Siebenmann¹⁷ in 35, and Pierce in 71 per cent of their cases.

Körner and Hammerschlag give a genealogic tree of five families in which forty-three cases of otosclerosis occur.

Arthritis Deformans.—Garrod's five hundred cases gave a family history of joint troubles in 43 per cent.

Osler's one hundred and seventy cases gave the same in 33 per cent, and he states that two or three children in a family may be affected.

RACE.

Neumann states that otosclerosis is much more common in the white race than in the negro, and Osler makes a similar statement regarding racial incidence about arthritis deformans.

CLIMATE AND CLIMATIC CONDITIONS.

Dryness and warmth are said to favorably influence the course of the disease in rheumatoid arthritis and chronic adhesive processes, and dampness and cold produce an injurious effect. With the exception of the benefit derived from being out of doors, climate has no influence over otosclerosis or osteoarthritis.

COURSE OF THE DISEASE.

Otosclerosis.—Lake, Milligan, Gray and Politzer say that the onset may be slow or rapid, the course progressive, though sometimes stationary for years, but may be arrested spontaneously with a fair degree of hearing.

Arthritis Deformans.—The onset may be slow or rapid, the course progressive, but in many cases, after involving two or three joints, the disease becomes arrested and no further development occurs.

SYMMETRY.

Both are usually bilateral, but one side is more advanced than the other in the slowly progressive cases. In the swiftly progressive forms early symmetry is the rule.

TROPHIC CHANGES.

Otosclerosis.—Lake gives the following: The external meatus is often large, due to change in the subepithelial tissues; the lining skin is polished, pale and devoid of cerumen; the eustachian tubes are large, with or without rhinitis sicca, the latter being frequently associated with otosclerosis. Less labyrinthine fluids or their entire absence in cases of long duration.

Politzer also mentions atrophy of the membrane, and the pale, dry condition of the external meatus, devoid of secretion.

Arthritis Deformans.—Changes in the skin and subcutaneous tissues, loss of hair, alteration in the nails, early localized sweats, followed later by cessation of this function over the affected areas, sensory and calorific disorders, wasting of muscles, cartilage and bone.

The trophic changes just enumerated are grouped under arthritis deformans by Osler and others, but Painter and Llewellyn-Jones seem to associate them exclusively with rheumatoid arthritis.

In many long standing cases of chronic hyperplastic otitis media, one finds a glossy, thin, flaccid, transparent membrane, through which the details of the inner wall of the cavum tympani can be discerned; the eustachian tubes are wide and free, and these are sometimes accompanied by a large, smooth, dry meatus, devoid of cerumen.

Are these trophic phenomena peculiar to chronic hyperplastic otitis media or to otosclerosis or to both? This question cannot be conclusively answered at present, but I think it is probable that cases of typical otosclerosis, like those of osteoarthritis, are not accompanied by any special trophic changes.

MORBID ANATOMY.

Otosclerosis.—Lake states that the earliest known change is a mucoperiostitis of the inner wall of the cavum tympani. In the cases in which the terminal lesions were examined, any or all of the following changes were found: The annular ligament had disappeared and was replaced by spongy bone, the cartilage which normally covers the footplate of the stapes and surrounds the oval window had disappeared and was replaced by new bone. Patches of osteoporosis occurred

in the labyrinthine capsule, osteophytes were found in the oval window, some of which were intratympanic and others intralabyrinthine.

Gray says that the disease begins by the absorption of bone, and the region most commonly affected is supposed to be above and in front of the oval window, and that the changes may occur in any part of the temporal bone or the ossicles or the bones of the head.

Yearsley points out that the annular ligament is widest at its anterior superior margin and that the greatest degree of movement occurs here, and that perhaps irritation and friction may be a determining cause of the greater incidence at this situation. It is interesting to note in this connection that Painter lays special emphasis on the greater incidence of osteoarthritis in the joints most commonly used by athletes.

Gray further describes areas of bone which undergo absorption by osteoclasts, and the deposition of new bone by osteoblasts, the affected areas being sharply differentiated from the normal bone. The annular ligament and cartilage disappear and are replaced by spongy bone which shows a strong affinity for staining reagents, this bone becoming dense later.

Arthritis Deformans.—The following is a summary of the morbid changes occurring in osteoarthritis as described by Painter:

The synovial membrane shows practically no change, except about spurs which form at the junction of bone and cartilage. There is no diffuse infiltration of the capsule, as in rheumatoid arthritis. The cartilage hypertrophies at the edges, spurs form by the ossification of cartilage, whose cells are arranged in columns like those of rickets, at the junction of diaphyses and epiphyses, and these spurs become dense bone later.

The pathologic changes observed by Painter in rheumatoid arthritis may be summarized as follows: The synovial membranes are infiltrated and thickened, villi form and may ossify. The involvement of cartilage is next in order of frequency, but first in the order of clinical significance. It undergoes thinning, loss of sheen, striation and erosion. The bone is last affected, there is loss of calcium content, the intratrabecular tissue is replaced by fat and fibrous tissue; the trabeculae stand out on section and are smaller and fewer in number. There is no evidence of necrosis.

Osler's description of the morbid anatomy of arthritis deformans is briefly as follows: The synovial membranes are thickened and fringes form, the periarticular tissues are infiltrated and swollen, the cartilage becomes soft and absorbed, or may disappear and be replaced by fibrous tissue of bone. The bone ends become smooth and eburnated in long standing cases, and the shafts atrophy.

New bone may form in the ligaments, especially in the spine, and may be followed by bony ankylosis, the latter occurring commonly in the vertebral joints, but rarely in those of the extremities. Muscles undergo rapid atrophy, and a radiograph shows atrophy and hypertrophy of bone and erosion of cartilage.

Ironside Bruce¹⁸ points out that in early cases of osteoarthritis, areas of translucency, sharply marked off from normal bone, can be seen by the X-rays.

It will be observed that Painter gives the pathologic changes of rheumatoid and osteoarthritis separately, whilst Osler gives them combined under the title arthritis deformans.

In rheumatoid arthritis the soft tissues undergo early proliferation, to be followed by atrophy, which also involves cartilage and bone. Hoffa states that bony proliferations, when they do occur in rheumatoid arthritis, are in proportion to the amount of atrophy that has taken place, and he would regard them as reparative. (Llewellyn-Jones.) In osteoarthritis the soft tissues are practically unaffected, but cartilage proliferates and goes on to ossification, with the formation of osteophytes. It has been observed that the new bone formation in cases of otosclerosis is more than sufficient to replace the old bone and cartilage which has disappeared, and no explanation is offered to account for this excess of new growth.

In my opinion the excess of new bone formation, as represented by osteophytes in any joint, is due to the proliferation and hypertrophy of cartilage at certain points, this hypertrophied cartilage becoming ultimately ossified.

The microscopic pathologic changes given by Gray in his lucid description of the morbid anatomy of otosclerosis are practically identical with the physiologic phenomena of ossification in any cartilage developing bone, from the osteoclastic and osteoblastic activity down to the greater affinity of the new bone for staining reagents.

DISEASES AND CONDITIONS SAID TO ACT AS EXCITING CAUSES
OF ONSET AND EXACERBATIONS.

The following list of diseases and other conditions have been mentioned as causes of onset and exacerbations in both affections: Syphilis, tuberculosis, gout, rheumatism, rickets, anemia, tonsillitis, exposure to cold and chill, inflamed processes in the nose, nasopharynx and middle ear, puerperium, pregnancy and lactation, anxiety, sorrow, depression and nursing the sick, excess of alcohol and tobacco, trauma and arteriosclerosis.

PATHOGENY.

The exact pathogenesis of otosclerosis and arthritis deformans is unknown, but many causes have been suggested, and these may be conveniently arranged under infective, nervous, vascular, metabolic and traumatic theories of origin, any or all of which may act by producing nutritional disturbances.

OTOSCLEROSIS.

Infective Theory (microbic).—Inflammatory middle ear processes (Katz,¹⁹ Habermann,²⁰ Scheibe,²¹ Ballenger²²).

Primary osteitis of the labyrinth capsule which is independent of middle ear disease (Politzer).

Syphilis, supported by Habermann, but disputed by Korner. Congenital syphilis is considered by Lake to influence onset.

Toxic.—Stucky, quoted by Kerrison, suggests that toxins resulting from errors of diet and circulating in the blood are important factors in the progress of the disease, if not in its causation.

Apparently against the infective view is the observation put forward by Gray, Politzer and Moos,²³ that otosclerosis occurs without any trace of middle ear inflammation, and that of Gradenigo as to its negative bacteriology.

Nervous Theory.—Anxiety, sorrow and depression have been suggested by Walb.²⁴ Walb also states that there is a greater tendency for otosclerosis to develop in individuals who are subject to mental affections and nervousness.

Vascular Theory.—Arteriosclerosis as a cause in some cases is suggested by Maupetit.²⁵ Habermann found the foci of the disease in the temporal bone, grouped around the blood vessels entering from the periosteum of the tympanum. Ane-

mia as a factor has been mentioned by Dundas Grant²⁶ and Gray, and the latter also describes areas of necrosis.

Metabolic Theory.—Puerperium, pregnancy and lactation. Bezold found otosclerosis associated in its onset with the puerperium in 18 per cent of one hundred and ninety cases. Politzer, Habermann and others have made similar observations.

Rickets (Politzer), gout (Tonybee, Buck and Argnano²⁷).

Ossification of cartilage cells around labyrinth capsule (Siebenmann).

Part of a general sclerosis of the submucous tissue of the whole respiratory tract (Lake).

Traumatic Theory.—Sudden explosions, or injuries to the cranium, may increase or cause sudden deafness in these cases (Politzer).

ARTHRITIS DEFORMANS.

Infective Theory (microbic).—Organisms found in joints (Bannatyne,²⁸ Poynton and Payne.²⁹ Occurrence of influenza and gonorrhea as antecedent affections. Onset soon after tonsillitis (Bloodgood,³⁰ Llewellyn-Jones, Bannatyne).

Apparently against this view are the observations of Painter and Odery Symes,³¹ who were unable to find organisms in the majority of the affected joints which were examined by them.

Toxic.—A toxic trophoneurosis (Tessier³²), an autotoxemia (Tubby³³), a cerebrospinal toxemia (Llewellyn-Jones).

Oral and alimentary sepsis have been suggested as the commonest source of the various types of toxemias.

Nervous Theory.—Worry, fatigue and depressing mental conditions. Changes found in the anterior cornua of the spinal cord (Folli,³⁴ Mott,³⁵ Bannatyne, Latham³⁶). Lesions found in the peripheral nerves of joints (Pitres and Carriere³⁷). The nervous theory is said by Stengel³⁸ and others to explain the articular changes, the muscular atrophy and the trophic disturbances in the skin.

Vascular Theory.—Arteriosclerosis is mentioned as a cause of osteoarthritis by Billroth,³⁹ Tessier and Lancereaux. Anemia is said to be present at the onset or during the course of the disease in osteoarthritis. Goldthwait is of opinion that the blood in osteoarthritis shows no special changes, and this view seems to be supported by the observations of Erving,⁴¹ who made a careful blood examination in twenty cases affected by the disease.

I am not aware that this point has been fully tested in cases of otosclerosis whose appearance indicate the condition of anemia.

Metabolic Theory.—Pregnancy, lactation, puerperium and the menopause, thyroid, ovarian and uterine disturbances. Loss of calcium content in the bones, and the greater output than intake of calcium salts during the active period of the disease in rheumatoid arthritis (Painter). That the disease is due to a condition of acidosis (Barr,⁴² King⁴³).

Traumatic Theory.—Godlee⁴⁴ states that a severe injury in youth may determine an attack of osteoarthritis later in life. Painter points out the frequency of osteoarthritis in the most commonly used joints of athletes.

LINES OF TREATMENT.

The same or equivalent lines of treatment have been suggested in both affections.

Otosclerosis.—

Drugs.—Pot. iod., iron, arsenic, thyroid and thymus extracts, phosphorus, mercury.

Injections.—Fibrolysin, vaccines, intratympanic oils, etc.

Mechanical and Surgical.—Pneumomassage, probe massage, stapedectomy.

Counter Irritation.—Blistering, etc.

Arthritis Deformans.—

Drugs.—Pot. iod., iron, arsenic, thyroid and thymus extracts, etc.

Injections.—Fibrolysin, vaccines, intraarticular injections of sterilized vaselin (Buedinger⁴⁵).

Mechanical and Surgical.—Massage, arthrectomy, cheilotomy (Handley and Ball⁴⁶).

Counter Irritation.—Cautery, blistering.

CONCLUSIONS.

The following are the conclusions at which I have arrived:

1. That chronic adhesive processes of the ear, or, as Kerison calls it, chronic hyperplastic otitis media, is rheumatoid arthritis affecting the organ of hearing.

2. That otosclerosis is osteoarthritis of the stapediovestibular articulation and of the bony labyrinthine capsule.

Dundas Grant has noted the frequent association of the two

diseases in the same individual, and the occurrence of osteoarthritis in the female progenitor of many of the subjects of otosclerosis.

3. That the morbid changes of chronic hyperplastic otitis media and rheumatoid arthritis are practically identical, and those found in typical otosclerosis are similar to those found in osteoarthritis and spondylitis deformans.

4. That as all the affected structures are developmentally, anatomically and physiologically alike, and when in these structures identical types of destructive and reparative changes occur, the natural inference to be drawn is that these processes are the result of a common pathogenesis.

It may be urged that it is incorrect to try and establish an analogy between other articulations and that of the stapes in the oval window, but I submit that the analogy is complete from every standpoint. The periotic portion of the temporal bone is developed in cartilage around the auditory capsule, and in this respect is similar to other cartilage bones. Anatomically, the similarity is also complete. In ordinary joints of the extremities we find bone covered by hyalin cartilage, and when a joint cavity exists, synovial fluid is present. Synovial fluid, according to Halliburton, is viscid, rich lymph plus mucinoid material. It is secreted by the cells lining the synovial membrane, and its viscosity is due to the presence of mucin. In the absence of a joint cavity the bony skeletal elements, for the purpose of greater stability, are linked together by fibrous tissue or fibrocartilage, as in the case of the vertebral column in the mid-dorsal or lumbar region. (There are small synovial cavities in the cervical region between the lateral portions of the bodies.) The stapediovestibular joint is similar to a mid-dorsal articulation. The osseous labyrinth is a cartilage developed bone, and hyalin cartilage is found round the margin of the oval window and on the edge and vestibular aspect of the footplate of the stapes. The bony labyrinth walls contain interglobular cavities enclosing remnants of cartilage (Yearsley, quoting Manasse.)

The annular ligament is a fibrous structure which holds the stapes in position in the oval window. The perilymph, according to Halliburton, is a viscid fluid, not pure lymph, as it contains mucin, which is the cause of its viscosity. Physiologically, a common joint possesses the double function of being a sense organ of relative position and an organ of locomotion.

The labyrinth contains a sense organ of relative position for the head and the organ of hearing, the latter depending for the conduction of sounds on a system of joints.

5. That when, in addition to the identity of morbid anatomy, we find a striking analogy between the two diseases in the points of age, sex, race, hereditary incidence, symmetry of lesion, trophic changes, course, associated diseases and conditions which are said to influence onset and exacerbations, pathogeny and lines of treatment, the above seems to me to be the only conclusion to which an unbiased observer can come.

6. That in all the morbid changes there are two outstanding features, namely, atrophy and hypertrophy, running side by side or alternating, the atrophy being an active process as well as the hypertrophy.

7. That in the case of chronic hyperplastic otitis media and rheumatoid arthritis we find the most marked activity of the disease in the soft or clothing tissues, which first undergo thickening, to be frequently followed by atrophy, the latter ultimately involving the supporting structures.

8. That in the case of otosclerosis and osteoarthritis the most marked activity of the pathologic changes is in the firm or supporting tissues, the cartilage undergoing proliferation and ossification, with the formation of osteophytic overgrowths. The juxtaposition of hyalin cartilage and bone appears to offer the most favorable anatomic site of election at which these morbid processes take place.

If this view is correct, the included remnants of cartilage described by Manasse as being present in the osseous labyrinthine wall afford the necessary juxtaposition of the two tissues, and would explain the incidence of the patches of otosclerotic disease found scattered throughout the petrous portion of the temporal bone.

9. That the essential pathogenic factor underlying an active atrophy and hypertrophy can be only one, namely, nutritional, although the conditions which may cause nutritive disturbances are manifold.

10. That as nutritional disturbances in tissues can be brought about by infective, vascular, nervous, traumatic and metabolic influences, either or all of which may be acting in any given case, it is, therefore, impossible to fit otosclerosis and osteoarthritis into one airtight, pathogenic compartment.

I am, however, of the opinion that the essential factor

underlying the morbid changes is a chemical one, affecting the nutritive stability of developing and fully developed bone and cartilage, comparable to the rachitic phenomena which occur in developing osseous tissues, but as to how these chemical disturbances are actually initiated, it is at present not possible to explain.

REFERENCES.

1. Painter: Amer. Pract. of Surg., 1907.
2. Kerrison: Diseases of the Ear, 1913.
3. Lucae: Progressiv. Schwerhörigkeit, Berlin, 1907.
4. Politzer: Diseases of the Ear, fifth edition.
5. Osler: Principles and Pract. of Med.
6. Keen: Textbook of Surgery.
7. Llewellyn-Jones: Arthritis Deformans, 1909.
8. Gray: Diseases of the Ear, 1910. Trans. Otolog. Soc., Vol. 7, 1906.
9. Milligan: Textbook of Diseases of the Ear.
10. Lake: Diseases of the Ear, fourth edition.
11. Garrod: Allbutt's System of Med., Vol. 3, second edition.
12. Pierce: Quoted by Yearsley.
13. Yearsley: Textbook of Diseases of the Ear, 1908.
14. Stewart: Quoted by Osler.
15. Bezold: Die Funktionel Prüf. d. menschl. Gehör.
16. Denker: Die Otosclerose.
17. Siebenmann: Zeitschr. f. Ohrenh., Bd. 34.
18. Bruce, Ironside: Quoted by Llewellyn-Jones.
19. Katz: Arch. f. Ohrenh., Bd. 53, S. 68.
20. Habermann: Arch. f. Ohrenh., Bd. 60, S. 37.
21. Scheibe: Verhandl. d. Deutsch. Otolog. Gesellsch., 1901.
22. Ballenger: Textbook of Diseases of Ear, Nose and Throat.
23. Moos: Quoted by Gray.
24. Walb: Schwartz, Handbuch d. Ohrenh.
25. Maupetit: These de Bordeaux, 1905.
26. Grant, Dundas: Trans. Otolog. Soc., Vol. 7, 1906.
27. Argnano: Rev. Hebdom. de Larynx, 1896.
28. Bannatyne: Rheumatoid Arthritis.
29. Poynton and Payne: Trans. Path. Soc., Part 2, 1902.
30. Bloodgood: Progress. Med., Vol. 4, 1907.
31. Symes, Odery: Rheumatic Diseases.
32. Tessier: Rheumatismes, 1908.
33. Tubby: Lancet, December 26, 1908.
34. Folli: 11 Policlinico, December, 1904.
35. Mott: Braine, 1902.
36. Latham: Lancet, April 6, 1903.
37. Pitres and Carriere: Arch. General de Bordeaux, 1898.
38. Stengel: Amer. Jour. Med. Sciences, 1903.
39. Billroth: Surgery, New Sydenham Soc. Transl.
40. Goldthwait: Boston Med. and Surg. Jour., 1904.
41. Erving: Amer. Jour. Med. Sciences, 1903.
42. Barr: Brit. Med. Jour., April, 1913.
43. King: Johns Hopkins Bulletin, 1907.
44. Godlee: Roy. Soc. Med., Clin. Sect., March, 1908.
45. Buedinger: Quoted by Tubby.
46. Handley and Ball: Brit. Med. Jour., May 13, 1913.