BONE GROWTH AND BONE REPAIR.*

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*LECTURE II.***RESEARCHES MADE BY SYME AND BY GOODSIR REGARDING THE
GROWTH AND REPAIR OF BONES.**

My last lecture closed with the death of Hunter in London in the autumn of 1793. We shall now proceed to Edinburgh, to see what two men who made Edinburgh famous in the middle decades of last century—Syme the surgeon and Goodsir the anatomist—can teach us regarding the manner in which bones grow and heal. It suits our purpose, however, before proceeding to Edinburgh, to discover how bone surgery stood in the North of England during Hunter's time.

No one who values a knowledge of the history of surgery and of learning in England can afford to be ignorant of Charles White of Manchester. He was born in the same year as Hunter, 1728; he was a class-fellow of his in the Covent Garden School; through his long life he never wavered in his loyalty to Hunter's splendid abilities. He was elected a Fellow of the Royal Society long before Hunter. Cullingworth has assigned to him a foremost place amongst British gynaecologists; Cunningham has given him equal rank amongst the pioneers of British anthropology. He took a leading part in founding the hospitals, colleges, and learned societies of his native city, Manchester.

We propose to make his acquaintance in April, 1768, when Edmond Pollet, a country lad of fourteen, presented himself at Manchester Infirmary with an abscess in the left shoulder, the disease having commenced suddenly a fortnight previously. Pus was issuing by several sinuses situated in the pectoral and deltoid regions. If Charles White, then in the prime of his professional career, had followed the standard treatment of the period, he would have amputated the arm; but he resolved to try and save the limb by adopting a novel and conservative method of treatment. Making a deep vertical incision along the deltoid region, he forced the upper end of the dead shaft of the humerus from the wound and cut it off. Later, a further piece of the shaft was removed—altogether four inches of it. The arm was placed in a sling, so that "the weight of the arm might counterbalance the contraction of the shoulder muscles." Movement was permitted, to secure a sufficient degree of mobility at the shoulder-joint. In four months, to Charles White's surprise, the upper end of the humerus had been reproduced; there was only one inch of shortening, and the arm could be freely used. In reporting this case to the Royal Society in 1769, White drew two conclusions: (1) That when a bone was removed, the arteries of the part had the power to renew it; (2) That the operation of resection had manifest advantages over amputation, and deserved serious consideration as an alternative measure.

Charles White's novel operation of 1768 merely involved the resection of dead bone. In 1783, Mr. Henry Park, surgeon to the Liverpool Infirmary, was in a position to announce a further stage in the progress of surgery—the possibility of excising diseased joints as an alternative to the amputation of limbs. We merely note here that each of these innovations in the treatment of diseased bones and joints demanded a more intimate and exact knowledge of the life and growth of bone.

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* Three lectures of a course on "Anatomical and Physiological Principles underlying the Treatment of Injuries to Muscles, Joints, and Bones," delivered at the Royal College of Surgeons, England.

Having thus seen the rise of 'conservative surgery' in the North of England in the later half of the eighteenth century, we pass on to Edinburgh to watch the practice and principles of James Syme. In his day Syme held the centre of the surgical stage; but it is only the early part of his career which interests us now—the struggling decade between 1823 and 1833, from his twenty-fourth to thirty-fourth year, when he was forcing his way up the Edinburgh surgical ladder. In 1825 there was sent to him a woman, Christian Laing, age 38, who had suffered from caries (tuberculosis) of the shoulder-joint for six years. Syme was brought face to face with the same problem as had been presented to Charles White fifty-seven years before—should he amputate, or should he resect the joint and thus try to save the limb? He chose the latter, and the woman did well. Resection as a defined operation for the relief of a diseased joint, was, as we have seen, first formulated in 1783 by Henry Park, surgeon to the Liverpool Infirmary, in a letter to Percival Pott; but the suggestion which moved Syme to adopt the operation came from a French source. Almost at the same time as Park was elaborating and applying the operation of resection to joints in Liverpool, Moreau, a surgeon in the North-East of France, was adopting a similar method of treatment, though it was many years later (1816) before his French colleagues recognized the value of his work. The first effort of Syme's youthful career was to introduce this operation into Scotland. In 1831 he published a *Treatise on the Excision of Diseased Joints*. By that date he had done fourteen resections of the elbow-joint. The introduction of a new surgical method invariably makes new demands on our knowledge of anatomy and physiology. The adoption of resection of joints as a routine measure made an exact knowledge of bone reproduction more urgent than ever.

If we would use words in a strictly conventional sense, we must describe Syme as eminently a practical as well as a daring surgeon. To the onlooker he seemed to apply a remarkably sound, common-sense judgement to the various surgical problems which came before him. In reality he was, as all purely practical men must be, an experimental surgeon, trying to discover the best means of treatment by roughly balancing the results which attended one method against those which followed from another. But for one brief period in his life Syme became a rational surgeon. In 1835—two years after he succeeded to the chair of clinical surgery in Edinburgh University—he had to treat the case of a young girl who suffered from acute osteomyelitis of the tibia. He had to amputate. When he dissected the leg, he found the shaft of the bone dead, and enclosed by a new stratum of bone which was adherent to, and apparently formed by, the periosteum. To settle for all time that periosteum could and did reproduce bone, he carried out the following well-devised—and, I have no doubt, neatly executed—experiment on young dogs.

In his first experiment he removed $1\frac{3}{4}$ in. from the radius of both right and left legs; on the right he also removed the periosteum, whereas on the left this membrane was preserved in place. When the dog was killed at the end of six weeks, the missing part of the left radius was reproduced; whereas, on the right, where the periosteum had not been preserved, a gap still remained. He repeated the experiment on a second dog, and got the same result: when the periosteum was removed, a gap remained.

He changed the conditions of the experiment. Taking another dog, he raised the periosteum from a segment of the radial shaft, and separated the periosteum from the bone by introducing between them a ferrule of tin-foil. The periosteum formed a layer of bone on the tin-foil.

Finally, he cut away the periosteum from a segment of the radius, and wrapped the denuded surface with tin-foil. No layer of bone was deposited on the tin-foil, because there was no periosteum covering it.

We have here the Haller-Duhamel controversy again raised, and it is clear Syme became a convinced Duhamelite.

We are now to make the acquaintance of a man who in his intimate and deep grasp of the problems presented by living matter came nearer to Hunter than any other Briton of the nineteenth century. In physical appearance John Hunter and John Goodsir were as different as men can be. Hunter was from the West, of medium stature, alert and fiery; Goodsir was from the East—from Anstruther in the county of Fife—tall, gaunt,

serious, and Calvinistic, with a long, sombre countenance. But Hunter and Goodsir were alike in this: they had an insatiable capacity for work, and an almost 'uncanny' gift of rightly interpreting, from the slenderest of clues, the more secret workings of living matter.

Here, however, we have to do only with Goodsir's investigations concerning the growth and reproduction of bone. Goodsir knew well about Syme's researches into the reproduction of bone by periosteum; he had 'dressed' for Syme; he was a student in Edinburgh and apprenticed to Nasmyth the dentist when Syme was rising to the height of his fame. There was every inducement for him to support Syme's conclusions; but the result of his investigations convinced him that the periosteum had no power to form bone, and that there was only one element in the body which could form and reproduce bone—namely, the corpuscles, which he had discovered and studied with his microscope as normal constituents in every variety of ossification. Goodsir was a Hallerite of a new kind.

No one can serve so well as Goodsir to bring home to us the transformation which took place in our knowledge of living bone in the decade which followed 1838—when men first came to realize that living matter is made up of units or atoms to which we give the name of cells or corpuscles. We are pursuing a straight path when we lay bare the circumstances which made Goodsir one of the pioneers of the cell doctrine. There are, in the first place, the circumstances of his training. He came of a line of medical practitioners. At the age of sixteen—in 1830—he was apprenticed to Nasmyth the dentist. He had the most delicate control of his long fingers, and very soon began to apply his manipulative ability to the investigation of tooth formation—which entailed a collateral study of bone growth. In Knox's dissecting-room he was thrown amongst the men who were to be leaders in science and in medicine—Edward Forbes, Fergusson, John Reid, and Sharpey. He dressed for Syme and dissected for Alison. In 1835 he became a Licentiate of the College of Surgeons of Edinburgh, and returned to Anstruther to assist his father. In three years he was back in Edinburgh in search of a foothold on the ladder which led to the more eminent posts in medicine. He had to wait until 1841, when he was twenty-seven years of age, before one came—the curatorship of the Museum of the College of Surgeons, at a salary of £150 per annum, out of which he had to pay an assistant. He only held the office for three years; but never did man crowd years with discoveries as Goodsir did these three. They were discoveries, we shall see, that have a very direct bearing on the problems we are exploring.

Goodsir brought to his office not only rare powers of brain and hand, but two qualifications which are absolutely essential for the man who would open a new field of knowledge—a new instrument and a fresh inspiration. The new instrument was the compound achromatic microscope, which had then been perfected by Lord Lister's father, and was Goodsir's companion from his boyhood upwards. His inspiration he drew from years spent in the study of the marine forms of invertebrate life which he dredged from the waters of the Firth of Forth. Molluscs, echinoderms, and sponges presented him with the same problems of life as did the tissues of the human body, but in a simpler form. He had the means of spanning the gap which seems to separate the hydra from the human body with much greater accuracy than was possible in Hunter's time. When he came to unravel the obscure and complex process of bone-building in the human skeleton, he found the clue from his work on sponges; they also build skeletons.

Goodsir was a follower of Hunter. In his youth he accepted Hunter's teaching that bone was deposited by arteries and was absorbed and remodelled by lymphatics. His microscopical investigations of the growing epiphyseal lines of bones revealed cartilage cells grouping themselves into serried ranks; he saw, or thought that he saw, these cartilage cells settle in the meshes of the cartilaginous trabeculae and become "bone-forming corpuscles"; he traced the transformation of the primary spaces in the cartilage from one stage to another until they became Haversian canals, still lined by the cells which he regarded as the descendants of the primitive cartilage corpuscles. He saw how the corpuscles of the Haversian canals became included within the bone to become its living denizens. He knew that similar cells built up the skeletons of invertebrate forms

of life, and had no doubt that the human skeleton was laid down, not by arteries, but by an element of which Hunter had no conception—separate self-acting units of living matter. That discovery—Goodsir made it for himself, others had done the same independently—marks a new chapter in our knowledge of bone. But the old or Hunterian chapter did not pass out of date; the new chapter merely gave a more precise interpretation of the facts contained in the old. Bone corpuscles were substituted for arteries.

There were in the Museum of the Edinburgh College, under Goodsir's care, certain famous specimens which had been made in William Hunter's school in London by Cruickshank. They were supposed to demonstrate that lacteals opened on the intestinal villi by open mouths. Goodsir applied his microscope to these specimens; he could see the injected lacteals in the villi, but nowhere could he find openings or mouths. He applied himself to the problem of absorption. He fed a dog, and when digestion was at its height, examined the villi. He found cells laden with the products of digestion, and concluded that the cells which line the bowel were the agents by which food was taken up and absorbed from the contents of the intestinal tract. His intimate knowledge of cellular processes in the lower forms of life led him further; he realized that every cell in the human body must have a power of absorption. Absorption was a natural function of every kind of cell—including those which are found in bone. Thus, he had to throw overboard Hunter's conception of lymphatic vessels playing the part of bone absorbers and bone modellers, and put in their place simple units of living matter—bone cells.

The microscope revolutionized, and at the same time simplified, our conception of the growth, maintenance, and reproduction of bone. In place of it being a living tissue manipulated by arteries and by lymphatics, it became an organization of living units—bone corpuscles—each of them endowed with the power to build up or take down that territory which lay directly under its control. Goodsir was the first to realize the new picture of bone. That discovery has not made Hunter's assumption of 'consciousness' in bone less tenable. How are such cells controlled? What are the circumstances which make them lay down bone on one day and carry it away on the next?

The investigations which Goodsir made on the nature of bone, during the three years of his curatorship, are recorded in four very brief papers which first appeared in his *Anatomical and Pathological Observations*, published in 1845.* One of these is entitled, "The Mode of Reproduction after Death of the Shaft of a Long Bone." It is an inquiry concerning the bone-forming power of periosteum—being an answer to Syme's investigations mentioned in an earlier part of this lecture. He concluded that periosteum has no bone-forming power—it is simply, as he terms it, a 'limiting membrane.' He did not deny that periosteum "participated in the office of regeneration—an important principle in surgery," but its power to form bone depended wholly on the proper substance of the shaft which had become adherent to it. By actual experiment he removed periosteum by scraping, and found particles of bone adhering to its deep surface. From such fragments, he concluded, new bone was reproduced. He examined the periosteal shells which form round necrosed shafts. He found that wherever there was a rough or ulcerated patch on the old shaft, there was also in the corresponding area of the periosteum a nucleus of bone growth; but where the areas of the old shaft were perfectly smooth—where there was no trace of exfoliation or ulceration—there was a gap or cloaca in the overlying periosteal shell. If the periosteum owed all its osteogenetic power to adherent morsels of bone, then these appearances were just as they should be. He conceived that the shaft of a bone might be killed so quickly by disease that there was no time for the separation of living fragments to act as bone grafts on the periosteum. In such a case there would be no reproduction of bone. If the greater part of a shaft did die, he observed that ossific centres shot out most vigorously from the terminal living parts. He had never seen an epiphysis take any part in the regeneration of a shaft; in a physiological sense an epiphysis should be regarded as a separate bone. Finally, as regards Syme's experiments,

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* See *The Anatomical Memoirs of John Goodsir*, by William Turner, Vol. ii., 1868.

Goodsir held that they did not demonstrate an osteogenetic power in periosteum, but they did demonstrate that, as detached by the surgeon, it could and did carry with it bone grafts which could serve as centres of reproduction. For Goodsir, a bone was a hive of bone corpuscles wrapped within a nest of periosteum.

I have mentioned Hunter's graphic and accurate picture of what the unaided eye can see when a living bone casts off a dead piece. Goodsir's paper on "Absorption, Ulceration, and the Structures engaged in these Processes" adds a fitting pendant to Hunter's picture—a pendant painted through his microscope—the earliest picture of its kind. We have seen that Goodsir recognized the corpuscles which lined the walls of the Haversian canals as the oldest and most active of the cellular constituents of bone. He had observed them on the surface of the bone, under the periosteum. He knew well that these canalicular cells could be stimulated to activity by inflammation; in Hunter's phraseology, they were endowed with irritability. He saw, in an inflammatory area of bone, that these cells multiplied in the Haversian canals; the walls of the canal widened by the proliferation of tissue and the absorption of the wall until neighbouring Haversian systems almost met, or did fully meet. He saw no impossibility in the cells which laid down bone changing their mode of life and devoting themselves to clearing away their old handiwork. He conceived that the more active these bone-devouring cells were, the shorter would be the term of their lives, and the sooner would they melt and their remains pass into the general circulation. By the proliferation of the cells in the canalicular systems an area of dead bone was separated from the surrounding living bone. The microscope simplified the understanding of the effects of inflammation on bone: Goodsir was the first to realize that these changes were effected by living units or cells.

Goodsir's bone researches were all carried out in the three years of his curatorship. In 1846, at the age of thirty-two, he was elected to the chair of Anatomy in the University of Edinburgh in succession to the third Monro. Just before the onset of his long, disastrous, and drawn-out illness, some ten years later, he opened up a field of research which yet remains to be explored. It is one which is destined to throw a new light on the living qualities of bone corpuscles. In 1853 a pupil had sent him a new form of sponge dredged from the waters off Spitzbergen. While investigating its structure, he observed that the spicules—its skeleton—had many forms, but each was built and laid down so as to strengthen and keep open the water-canals on the entirety of which the lives of the sponge colonists depend. He looked for the builders and found them. No one had seen or studied them before. He formulated the following law: "A spiculum is formed by a series of sponge-particles (sponge cells), so arranged in a column or system as, by the silicification of more or less of their contiguous surfaces and substance, to form a continuous rod." In short, he saw groups of spicule-forming cells marshal themselves into a geometrical pattern and lay down supports of the exact form and in the exact position where such supports were needed. We shall see that bone corpuscles have also similar qualities.

During the last ten years, Professor Dendy,* of King's College, London, and his former pupil, Professor Woodland,† have carried out a series of researches which justifies one in regarding the scleroblasts which form the spicular skeletons of invertebrate forms of life as the exact counterparts of the osteoblasts of our own bodies. In the more primitive types a spicule is actually formed inside the cell—an intracellular secretion; all stages between the intracellular and extracellular mode of spicular formation can be demonstrated. The scleroblasts are special cells derived from the dermal layer. They do their work according to the needs of the animal frame of which they form part; they build their spicules so as to strengthen that side of a sponge which is exposed to the force of the waves, just as osteoblasts built to withstand the pressures applied to bone. The scleroblasts, Professor Dendy observed, are sensitive to vibrations.

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* For Professor Dendy's latest paper, see *Proc. Roy. Soc.*, 1917, lxxxix, 573.

† *Quart. Jour. Microscop. Sci.*, 1905, xlix, 231; 1906, xlix, 533.