An Address

ON

THE STUDY OF NATURE AS SHEDDING LIGHT
ON THE STRUCTURE AND FUNCTIONS
OF MAN.THE ANTLER OF THE DEER AND ITS RELATION
TO THE GROWTH OF BONE.DELIVERED AT THE SIXTH MEETING OF THE INTERNATIONAL
SOCIETY OF SURGERY.

BY

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IN the name of the British Section of the International Society of Surgery and its local committee it is my privilege to extend to our international colleagues a very hearty welcome. We are not unmindful of the courtesy, kindness, and hospitality with which the British members have invariably been received in the countries where the Congress has already met—three times in Belgium, once in the United States of America, and once in France. It will be the endeavour of the British Section to make our colleagues from beyond the seas feel "at home" in our midst, on this the first meeting of the International Surgical Society in Britain.

One of the tragedies of the war was the disruption of intellectual co-operation between the contending peoples. The work done in one country is often complementary to that done in others, and the collaboration of the scientific workers of all nations forms a powerful stimulus to the spread of enlightenment throughout the world. It is for the general good that endeavour be made to resuscitate and sustain the intellectual life of Europe by international co-operation, especially in the ever-active and boundless realms of science.

In a recent address given by me the question was raised whether the medical profession did not concentrate their studies too much on human phenomena to the exclusion of life as a whole. "The so-called divisions of Nature are purely arbitrary conveniences, having no existence except in our own minds, for, after all, we are but a bit of Nature, and everything pertaining thereto must have a bearing on humanity." Investigation into comparative anatomy and physiology tends to illuminate the obscure problems of growth of structure and function in man, and, as an illustration of this in one small field, attention is directed to some of the phenomena attending the growth and shedding of the antler of the deer, especially in its histological aspects, and the bearing which these have upon the growth of bone in man and other mammalia.

The male deer produce annually, within the period of three months, antlers of solid bone, which in some species grow to immense size. They carry these antlers for a few months, then shed them, and repeat the process every season. The antlers are branched outgrowths from the frontal bones of the skull, and are amongst the most remarkable and interesting instances of sexual dimorphism. The yearly recrescence takes place chiefly from June to August. Not only does the bone grow within these few months, but the whole antler is enveloped from base to tip by the velvet, which keeps pace with the rapid growth.

The Velvet: its Function.

There is very little insolation between the vessels of the velvet and those of the bone in the antler. Besides supplying through its blood vessels heat and moisture and giving general protection as a cuticular covering and limiting membrane, the highly sensitive velvet serves at least two purposes, one to the antler itself and one to the animal as a whole. It protects the soft pulpy growing antler by causing the animal to eschew issues of combat and violent or even slight contact with foreign bodies. In

this way wounds of the antler with their attendant haemorrhage and risk of septic or pyogenic infection are prevented. Were it not so protected the pulpy antler might be burst, ruptured, or torn, and, being highly vascular, so much blood might be lost as to endanger the life of the animal.

When the osseous matter in the antler has solidified there is no further need for this covering, which has already served its purpose. The growth of the bone at the corona compresses the blood vessels of the velvet and cuts off their blood supply, when the whole velvet withers, becomes dry and shrivelled, is cast off in ribbons or is stripped like a discarded glove. The solid antler now remains—a formidable, insensitive weapon.

What is the Cause of the Annual Shedding of the Antler?

As one of the secondary sexual characters, the antler is usually described as merely an ornamental weapon. It is, however, more intimately correlated to the sexual function. Though the reproductive organs with their interstitial tissue are the *fons et origo* of the antlers, the antlers, through the velvet, have a periodic reflex influence on the function of the testes. The phase of evolution and greatest sensitivity of the velvet corresponds to the period of minimal testicular activity as if a reflex inhibitive influence was exercised on the testes through the nerves of the velvet.

When the antler has become well formed and sclerosed, the nerves and blood vessels are obliterated, and the velvet is shed. At this period the bloodless, nerveless, insensitive structure is left as a weapon fit for combat. If, however, the velvet is to serve the retardative function over the reproductive organs, then it must be shed annually and grow afresh. The sensitivity of the antler at that early stage is thus probably purposive and is one reason for the antler being deciduous.

Two Points regarding the Structure of the Velvet:

- (1) The stratum lucidum—has it an independent vitality?
- (2) The cutis of the velvet grows directly on the bone.

With regard to the structure of the velvet, with its complete cutaneous investment containing glands, hair follicles, and appendages which are evolved with the rapidity and completeness of an embryonic structure, there are two points worthy of note from their bearing on surgical pathology.

First, the stratum lucidum is more advanced in development during the growing period than the stratum Malpighii, the former appearing mature when the latter is still embryonic; osseous tissue is first rapidly covered by stratum lucidum, the stratum Malpighii following. This corresponds with what is found in wounds, where the stratum lucidum penetrates blood clot and advances almost *pari passu* with the leucocytes, ahead of the stratum Malpighii, or on granulation surfaces where the stratum lucidum precedes the Malpighii, forming the "dry, red line" seen at the margin of a healing ulcer.

May not the question be raised whether the current view be correct—that all the layers of the skin grow from the stratum Malpighii upwards, and that the superficial layers, including the lucidum, are in process of being cast off as more or less effete? Would effete cells be the first to regenerate?

The evidence adduced tends to indicate that the stratum lucidum possesses an independent vitality and is endowed with the power of more rapid surface extension than the deeper layer. This also obtains when the stratum lucidum is detached from the body and is grafted on to a granulation surface. It is of importance to have this layer of stratum lucidum, thin as it is, covering a wound, as it forms a living barrier to the ingress of germs, and, once formed, the proliferation of the slower stratum Malpighii and the organization of the tissues inside the wound proceed apace. The deep cutaneous layers, however, provide a thicker covering for the wound and protect the interior from friction and injury.

The second point is that in the antler one sees the cutis

of the velvet growing directly on the bone without any intervening membrane (periosteum), the cells of the cutis resting on the osseous tissue contiguous the one with the other. The cutis is sessile on the bone. Analogies may be found in the human body under pathological conditions. It may be seen in exposed bone, in compound fractures of the tibia, with loss of soft tissues. The skin may then grow directly over the embryonic osseous tissue in the course of its formation, and, becoming rigidly attached, form an adherent cicatrix. The same may occur after amputations which have healed by granulation tissue, the skin becoming fixed to the osseous tissue, much to the detriment of the patient.

When an amputation has been performed in childhood through an arm or thigh, in the course of years, if the soft tissues are allowed to contract from disuse atrophy while the bone continues to grow, a conical stump may result. The bone gradually protruding through the soft tissues is covered only by a thin, stretched layer of cutis—chiefly stratum lucidum. Like the velvet in the antler the human skin tries to keep pace in covering the growing bone in its protrusion, but, unlike the velvet, it only succeeds in covering it by such a thin layer of closely adhering skin that it is liable to injury on slight occasion.

The Methods of Growth of the Antler—Analogous to Diaphyseal Bone.

The frontal bone from which the antler springs is not the usual site of diaphyseal bone. The frontal is only covered by pericranium, to which even the "Orthodox School" does not assign osteogenic powers of a high order. The method, however, by which the stag's antler grows from the pedicle, though not identical, is somewhat analogous to the growth of a diaphyseal bone, emanating from a single epiphysis, there being no distal apposition or impediment to its growth. Notwithstanding the myriad of cells so rapidly produced within there is no jumbling or overcrowding, each one forms and takes its proper place according to hereditary behest.

Protoplasm is not a single homogeneous substance. It is complex, each particle holding fast through countless generations to its own particular type. The cell also is not merely the expression of a chemico-physical basis of life, but every particle of living protoplasm within it has a long hereditary history fixed in the structure of each of its various molecules. So that, in the swarming millions of cells within the antler, each one follows by hereditary law its ordered sequence.

Metchnikoff's Belief as to Cause of Old Age and Death in Cells of Body Generally.

Metchnikoff believed that in the body generally old age is not brought about simply from the arrest of the reproductive power of the cells, but that the cells of the body grow old on account of the impairment of the phagocytes and the invasion of the body by germs introduced through the large intestine. In this way senescence, decay, and death occurred.

The Method of Death of the Cells of the Antler.

In the deciduous stag's antler none of these factors obtain. The whole evolution, ultimate sclerosis, death, and separation of the antler is aseptic, and phagocytosis plays no part therein. The death of the bone is primarily due to increased osteoblastic formation encroaching centripetally on the lumen of the vessels, resulting in sclerosis of bone, and finally in ischaemic death. The osteoblasts extract from the blood the ossein, which they deposit in their periphery and build themselves in, cut off their food supply, and become entombed.

There is no senescence in the cells of the antler—they all die young. The mature period of osteoblastic formation is just reached and the completed bone cells formed when they, while still in the full vigour of youth, perish by their own reproduction. For them there has been no senility and no decay. They have built up a beautiful structure, and when they perish they leave behind a nerveless, bloodless, hard, dense bone as a weapon of offence and defence, which can bear without sensation the blows of adversaries.

Why does the Osteoblast not Continue to Grow in the Antler Indefinitely?

There is no physical obstacle to an upward expansion of the antler. The rejuvenation of the cells of the antler depending on the increase of nuclear material is abundantly evidenced in nuclear budding, and even in the possible formation of new cells produced by the shedding of nuclear buds, surrounded by a layer of cytoplasm—daughter cells—an extra method of cell production augmenting the ordinary cell division.

Though contrary to recognized methods of cell proliferation, the phenomena of nuclear budding and the possible production of daughter cells is suggestive of a supplemental mode of cell production. Such would aid in the rapidity of cell formation and in the rejuvenation of the cells exhausted by constant segmentation and requiring to make still further effort to multiply at a point so far removed from their base—the pedicle.

The nuclear budding and the formation of daughter cells—formed and thrown off—may mark the commencement of a new cycle in cellular proliferation (being physiologically comparable to the period of sexual maturity in multicellular organisms); in this way senescence in the cells is warded off and rejuvenescence is maintained.

The Growth of the Osteoblasts outside of the Bone such as takes place after Fracture.

In the outpouring of osteoblasts in the repair of bone bereft of its periosteum, such as in fracture, the same question arises in an intensified form, as the osteoblasts are then outside of their own direct nerve control. Why do the regenerating cells which have been actively proliferating know when to stop their reproduction? Why don't they go on producing indefinitely? Here heredity cannot play the same dominating rôle, as the factors are so variable and accidental circumstances are introduced which the osteoblasts must overcome. There must be conditions governing the product of the outpouring beyond the influence of the trophic nerves of the bone—which, however, may still have a "wireless" control of the osteoblasts, or which may have a limited, independent life within the living tissue.

It is observed that as long as the osteoblasts which have thus been poured out can be kept in their germinal state fixation by ossein and consolidation is warded off and reproduction of cells is continued. Constant movement of the parts is conducive to large outpourings of cells, which are prone to take on the cartilaginous formation and fixation is delayed. An abundant supply of thin-walled blood vessels greatly facilitates the deposition of ossein and so encourages fixation.

Reference may be made to the case of a seaman who got his thigh bone broken in its upper third aboard a vessel wrecked in the Bristol Channel. He was tied to a spar, and, being washed overboard, got stranded on a rock, his damaged leg swinging to and fro in the waves for forty-eight hours. He was afterwards rescued and lay in hospital for many months. As a result of the constant movement to which his leg had been subjected by the waves, a great tumour-like mass of bone formed in the thigh in the midst of the torn and lacerated muscles; for the relief of this he was ultimately sent to me. So great was the development of new bone that an extensive "quarrying" with chisel and mallet was required before the normal shaft was exposed and alignment could be effected. After operation rapid healing took place with only an inch of shortening.

The Mature Osteoblast—A Typical Form of Cell.

A definite form or type of cell is recognized in the mature osteoblast of the antler. This is contrary to the opinion held regarding the mammalian osteoblast in general, which is said to be only definable by function and not by any special histological character.

When this cell was first seen by me in sections, from the growing antler, it seemed so distinctive as to appear *sui generis* to the antler itself. Many sections from various parts of the antler were subsequently studied to investigate the origin of the osteoblast and to trace it through its evolutionary stage from the germinal layer until it assumed its mature form.

Once the osteoblast assumes its mature form it becomes distinctive and the cell may be easily recognized and traced through its further evolution into bone. The typical form of the mature osteoblast is an ovoid cell with its nucleus situated peripherally and occupying its narrow end. In the antler one sees the mature osteoblast in great numbers all along the growing line. They are in such quantities that in many places they are obtrusively evident; though coincident with or in immediate sequence to attaining maturity, however, the osteoblast assumes the function of abstraction from the blood and deposition of ossein within a circumscribed area round itself. This forms a fuliginous veil of ossein quickly obscuring the cells and rendering the tissue opaque.

After recognizing this mature form of osteoblast in the antler of the deer, sections of growing bone from other animals were re-examined and were found to exhibit the same typical form of mature osteoblast, though they were not present in such numbers as in the antler. Thus they were seen in the growing epiphyses and in repair of bone in man, especially in children and in young adolescents, and in the growing epiphyses of the dog and other animals. The sections taken from bone growth in glass tubes also show the type of mature osteoblast somewhat similar to that seen in the antler. They may also be seen in bone growing in a cicatrix in the midst of the abdominal muscles—being carried there by the blood stream.

Two Forms of Ossification Found in the Antler at the Same Time.

This mature type of osteoblast may be recognized and followed through both forms of bone formation—the direct or membranous and the indirect or cartilaginous—though in the former it is more difficult to discern, as the ossein is deposited more quickly, thereby producing obscuration followed by rapid osseous fixation. These two forms of ossification are found in the same antler at the same time, and each proceeds through the same base, which is cartilaginous—a primary cartilaginous evolution.

In the human epiphyseal cartilage one finds two distinctive forms of osteoblasts placed back to back and contiguous to each other—the one destined to form epiphyseal cancellous tissue, the other dense diaphyseal bone.

The difference between the method of ossification in the antler and that of the mammalian epiphyses is that in the latter there are, in the epiphyseal plate, two layers distinct from each other—the one composed of diaphyseal cartilage, the other of epiphyseal cartilage. They go in different directions—the one toward the joint, the other away from it; whereas in the antler both forms of ossification pass through a common cartilaginous base, and after doing so the emerging cells become differentiated, the membranous ossification showing itself especially toward the distal aspects of the tines.

Bone Only Grows from an Osteoblast: the Osteoblast Breeds True to Specific Type of Bone.

It is held and taught by some histologists that all forms of mesoblastic tissue are intraconvertible—that a primitive connective tissue cell may develop into perfect fibrous tissue at one time, or into aponeurosis, cartilage, or bone at another—a kind of indifferent tissue capable of transforming itself as occasion requires.

From my observation there is no evidence of the existence of such an indifferent or elusive tissue, and none of an osteoblast being converted or being convertible into fibrous tissue. Periosteum never produced, nor is it capable of producing a single osteoblast. The bone cell is derived from tissue which is primarily osteoblastic and which produces nothing other than osteoblasts. Not only so, but besides being generically bone cells, the osteoblasts are produced according to the specialized type of bone to which they belong. A diaphyseal osteoblast produces diaphyseal tissue, and an epiphyseal osteoblast always epiphyseal tissue. The osteoblast breeds true to its specific type.

In the canine species it would be as natural to expect that there existed a generic canine cell, which was so indifferent to specialization that it could develop into a fox-

terrier or into a sheep-dog as chance or caprice might direct, as to believe that a single bone cell could be so indifferent to the behests of heredity as to produce a diaphyseal or an epiphyseal bone on demand.

The thousand memories of the atoms comprising each osteoblast make it always breed true to type. The cell observes the same adhesion to type in response to the demands necessitated for repair following injury of pathological change in the bone. What a difference in the bone formation produced by each! The diaphyseal is robust in regeneration and vigorous in pouring out the osteoblastic embryonic tissue or callus which forms an abundant splintage for fractures. The other is very economical in its response to injury, just issuing sufficient ossific substance to cement the damaged parts. What a blessing it is so, for, were the epiphyseal cells as vigorous in bone production as the diaphyseal, innumerable stiff joints would result from injuries, particularly as there is no limiting membrane at these points. How we humans are controlled by little things! If these minute cells did not breed true, slight injuries would result in stiff joints, and our national game of football, for instance, would be imperilled! If the intramembranous parietal bone were as vigorous at repair as a diaphysis, the new-formed bone masses might press upon and injure the brain.

Can a Living Osteoblast be carried by the Blood Stream?

If, from traumatic or pathological cause, a living osteoblast gains entrance into a blood vessel, can it be carried by the blood stream to a distance and be deposited within the body in some structure other than osseous, and, if so, can growth of bone result therefrom?

Experiments were tried to test this possibility, but the difficulties of isolating and handling such a minute structure and our clumsiness in manipulation rendered them abortive. While still pursuing investigation, however, Dame Nature, with her delicacy of touch and inimitable ways, performed the experiment and presented a beautiful illustration of the possibility of the fact that the blood stream can carry osteoblasts to at least a short distance and deposit them in blood clot, where they may grow and reproduce themselves, forming bone. Already it has been recognized—from experimental inquiry into the growth of bone, inside of glass tubes placed in the living tissue, which became filled with blood clot and serum—that the osteoblasts from the bone placed therein proliferated and penetrated the blood clot, the latter becoming slowly absorbed.

The experiment which Nature performed occurred in a man who had sustained a fractured humerus: a spiculum of bone from the interior of the shaft penetrated the brachial artery and allowed the blood to escape into the tissues and partly to return into the vessel through the rent in its wall. The blood, in its escape, flowed over the bare fractured bone, and osteoblasts, as they formed on its surface, would not only be laved by it, but some might be detached by the force of the stream. Six weeks after, when the patient presented himself to me, an aneurysmal swelling was found to have formed in front of the humerus, limiting flexion at the elbow. The swelling was dense and inelastic, with very little pulsation, though pulsation had been a marked feature of the swelling at an early period after the injury. In the fibrinous layer in the periphery of the sac there were plaques of new osseous tissue of varying thickness, which covered a considerable portion of the circumference of the aneurysm. These had evidently formed from the osteoblasts which had issued from the fractured shaft, and especially from the spiculum of bone which had penetrated the coats of the artery.

The osteoblasts had become peripherally distributed and entangled in the meshes of the fibrin formed from the coagulated blood. In this instance the osteoblasts were conveyed by the blood stream for a short distance only, measured by one or two inches, but it established the possibility that living osteoblasts, in favourable circumstances, may be detached from a naked bone in process of regeneration and may be conveyed by the blood stream to a distance, and there grow and produce new bone.

If the osteoblasts, in peculiar circumstances, could be driven into the lumen of the blood vessels, the stream could carry them and deposit them in internal organs where they

might produce osseous infarctions. It is fortunate that such a series of circumstances favourable to the transference of osteoblasts from one place to another by the blood stream seldom occurs.

The mature osteoblasts are of a size that does not render their transference by the blood stream easy, but if nuclear budding occurred and some of the minute buds covered with cytoplasm—daughter cells—were detached, their minute proportions would facilitate conveyance.

Instance of Osteoblasts conveyed by the Blood Stream and deposited in the Cicatrix of a Laparotomy Wound.

That bone sometimes forms heterotopically in the midst of the soft tissues and in the muscles is well known, and these instances are generally the result of accidental osteoblastic distribution following upon injury to bones and the tendinous expansion of the muscles inserted into them.* Besides this, however, it is possible that osteoblasts in their germinal stage may be carried by the blood stream and may be localized by injury with extravasation of blood—in the same way as germs circulating in the blood stream may be located. An instance which bears this interpretation has just occurred, and has been communicated to me by my colleague Professor Muir, pathologist to the University of Glasgow, who has also given me some of the sections—which my colleague Mr. MacRae, whose case it was, gives me liberty to use.

The new bone was formed in a cicatrix in the midst of the abdominal muscles, at the site of a laparotomy wound made seventeen days previously. There had been no bone present in that tissue at the time of the operation.

It is probable that the original tumour in the intestine of the patient was one that secondarily involved bone, and that some of the osteoblasts had gained entrance into the blood stream and had been deposited at the site of the extravasation—the laparotomy wound. It is interesting that the typical mature form of osteoblast is seen in the bone sections situated in the cicatrix in the midst of the abdominal muscle.

Miniature Antler: Bone grown in Glass Tube inside of Tissue.

The bone grown in the glass tube experiments resembles in miniature the growth of the antler. The bone grown in the tube receives all its blood supply from its base in the pre-existing bone. The main artery of the bone in the glass tube passes up the centre, sending out branches which subdivide into capillaries, which are seen most abundantly at the periphery next the glass of the tube. It is round the thin-walled vessels that the osseous tissue first forms. Though generally these thin-walled capillaries intervene between the new bone in process of formation and the glass, yet in some places the osteoblasts are in actual contact with the glass, in the same way as the osteoblasts in the antler of the deer come into immediate contact with the dermal covering (the velvet) without the presence of any intervening membrane. There is here no periosteum—except the glass which acts the part of a limiting membrane. There is, therefore, no peripheral blood supply; it gets all its nutriment from the base, yet the bone thrives and grows rapidly and abundantly. The soft tissues surrounding the glass tube supply the proper temperature to facilitate the growth of its osseous contents, thus taking the place of the velvet in the antler of the deer.

The Silver Ring Experiments and Deductions from them.

Duhamel in 1739 placed a silver ring round a bone under the periosteum in a living animal and found some time after that the ring had become covered by bone. He inferred from this that the periosteum secreted bone, and his experiment and deduction therefrom have been accepted ever since, and have appeared in many of our textbooks during the last 184 years as one of the cogent reasons for our belief in the osteogenic functions of the periosteum.

The result of the experiment was correctly observed, but the deduction drawn therefrom was wrong and illogical. It was based on a single premiss. It has been demonstrated

by me that when the periosteum has been removed from the bone and silver rings are placed on the naked *growing* shaft, the new peripheral osteoblasts emanating from bone rapidly form over the nude surface and completely cover the silver rings, enclosing them in a mass of bone—greater than would have formed had the periosteum remained intact.

Whatever views one may hold regarding the osteogenic function of the periosteum, it is hoped that in practice no one would sacrifice an otherwise healthy bone merely because the periosteum, from traumatic or pathological causes, happened to be removed. As long as the nutrient vessels maintain the blood supply to the diaphyses, the shaft of the bone will live, grow, and function.

Even portions of detached living bone severed from all blood supply, preserved aseptically and replaced among the tissues in suitable conditions, have a probability of life. The osteoblasts of the detached bone receive sufficient pabulum from the blood serum until the fresh vessels of the part penetrate the bone and bring nutritive relief. New osteoblastic formation in the shape of a vigorous germinal layer ensues and quickly consolidates into new osseous tissue which aids in fixing the detached bone in its proper place and afterwards in performing the function of the shaft.

Recognition of these facts will prevent the removal of useful, although "bare," bone, and limbs may be saved that would otherwise be sacrificed.

Bone Grafting: Report on Earliest Case.

Nude bone has been grown heterotopically in various parts of the body—such as in the vicinity of the great vessels in the neck, in the muscles of the extremities, in the body cavity attached at the omentum, etc. Young, growing, nude bone may be transplanted, and it will live and grow in its new situation and will form part of the body of man, becoming homogeneous with him.* Forty years ago this was demonstrated,† and since then bone grafting and transplantation have been frequently employed, especially during and since the great war. Many surgeons at home and abroad have used it very successfully and extensively, none more so than Morison of Newcastle.

Reference may be made in passing to the earliest cases of bone grafting in order to report their present condition, as sufficient time has elapsed to demonstrate, more nearly than the recent cases, the ultimate results obtained.

The first was one in which a boy, aged 3 years, came under observation after he had suffered for several months from pyogenic osteomyelitis of the humeral shaft, the dead, blackened bone of the arm lying loose inside the remnant of the periosteal sheath lined with granulation tissue. The loose dead bone was lifted out. As belief in the periosteum as a bone producer was at that time still in vogue, it was hoped that some portions of the bone might form from the periosteum. This did not take place, and the wound healed, leaving an arm without a shaft. One year afterwards the mother returned with her boy, desiring that the arm be amputated, as she said it was not only useless but required the sound arm to look after it. The shaft of the bone had not grown. He had neither a fulcrum nor a lever, and when he attempted to flex the forearm on the arm the muscles and soft tissues of the arm contracting wriggled like a loose hanging rope, the forearm dangling helplessly at the end of it. Instead of acceding to the mother's request to amputate the arm, bone grafting was resorted to. The humeral shaft was restored by the introduction of young growing human bone, removed for the correction of deformity from the tibiae. Six pieces of bone—one each from six different legs of three different persons—were divided into small fragments and were inserted between the muscles of the arm where the shaft ought to have been. These fragments became firmly united to one another and to the epiphyses so as to form a solid shaft. It supplied the fulcrum and lever, and enabled the arm to function, the bone growing along with the growth of the body—but not quite proportionately to it. The greatest growth occurred subsequently, mainly from the proximal epiphysis which had been preserved in part,

* Macewen: *Growth of Bone*, 1-12.

† Read before the Royal Society, London, May, 1881, and published in the *Proceedings of the Royal Society*, and also in the *Comptes Rendus de l'Académie des Sciences*.

* See instances in the volume on *Growth of Bone*, by Macewen, published by Jas. MacLehose, Glasgow, 1912.

while there was no growth from the distal epiphysis, the growing plate having been destroyed. The grafted part had somewhat increased in length and also markedly in thickness during ensuing years. While originally the grafted portion was in the centre of the arm, it was pushed toward the distal portion owing to the more vigorous growth from the proximal epiphysis. The arm is shorter than its neighbour, and no one would take it for an artist's model, but it has been of great service to its owner. Since manhood he has been able to maintain himself and his family by his own efforts—first as a joiner, then as laboratory attendant—and also, he has been able to go to the front and do his bit for King and country during the great war.

For the restoration of the lower jaw, grafting and transplanting of bone has been frequently successfully employed by many surgeons (especially in Froggall), restoring thereby the symmetry of the face, and, with the help of the dentist, the function of the lower jaw. In two such cases, operated on over eighteen years ago, the mandible has increased in size and strength commensurate with the rate of growth of the face, leaving little trace of the hideous deformities from which the patients would otherwise have been doomed to suffer.

One has endeavoured to give a glimpse into some phases of the comparative anatomy of the antler of the deer. Were one able to extend one's vision into other spheres of animal life, not only would they prove of absorbing interest intrinsically, broadening one's views, but they would shed fresh light on human structure in evolution and repair.

As to Nature as a whole, we are still in deepest darkness. Isn't there within each of us a mystery which has never yet been fathomed—a mystery which man shares in common with the minutest speck of primordial protoplasm of the wayside pool? The further we penetrate into the depths of Nature, the more numerous are the paths which are revealed for our searching, and to our finite eyes seem illimitable. Yet, in our search there are at least two things which we may find—one, not the extent, but a measure, of our abysmal ignorance; the other, that if we pursue our quest with a single purpose in search of truth for truth's sake only, we may get a glimpse of the spirit of Nature and feel the touch of The Hand that weaves the woof.

NORMAL AND MORBID CONDITIONS OF THE ADRENALS IN 100 HOSPITAL AND ASYLUM CASES;

WITH SPECIAL REFERENCE TO DEMENTIA PRAECOX.*

(With Special Plate.)

BY

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INTRODUCTION.

In making *post-mortem* examinations at the London County Asylums I (F. W. M.) had long been struck with the frequency with which I found small suprarenal capsules in cases of dementia praecox as compared with general paralysis. I have already shown a regressive atrophy of the testes and ovaries in dementia praecox, and compared the conditions found in one hundred cases of each dying in hospitals and asylums.⁵ There are many physiological and pathological facts showing the correlation of the reproductive organs with the cortex of the suprarenal gland, therefore it would not be surprising to find a diminution in weight of these glands.† There are certain clinical symptoms in

dementia praecox which show the probability of the correlation of a morbid change in the medullary portion of the gland—namely, low blood pressure, feeble pulse, cold extremities, acrocyanosis, shallow breathing, low oxygen consumption, and katatonia. Dr. G. H. Rae Gibson,¹⁶ working at Claybury at my suggestion, investigated the blood pressure in various types of insanity, especially in relation to the above clinical signs of dementia praecox.

Table of Average Blood Pressure in 143 Cases.

	Males.		Females.	
	Average Blood Pressure.	Average Age.	Average Blood Pressure.	Average Age.
Dementia praecox katatonia ...	113	28	111	28
Dementia praecox hebephrenia	118	30	114	27
Dementia praecox paranoia ...	113	35	125	43
Epilepsy	120	36	123	39.5
General paralysis	138	45	123	44.5
Congenital imbecility	115	21	109	34.5

I should not attach much importance to the results of the average blood pressure in these various groups, for where the difference is great—for example, dementia praecox and general paralysis—the age factor might be cited as the causal relationship of the difference. But on examining the tables in which the blood pressure of each of the 143 cases is given, one finds that in 10 of the cases of katatonic dementia praecox, and in 4 of the 27 cases of hebephrenic dementia praecox, the blood pressure is under 100; whereas in the 12 cases of epilepsy, in the 15 cases of general paralysis, and in 9 of the 10 cases of congenital imbecility, there is not a single case in which the blood pressure is under 100; moreover, in 5 out of the 10 cases of katatonia, and 2 out of the 4 cases of hebephrenia, the blood pressure was very low—under 90. In not one of the cases of general paralysis was it under 120. These observations were made before I undertook the investigation of the reproductive endocrine system of glands.

Dr. Dawson, assistant medical officer at the Maudsley Hospital, undertook last year, while assistant medical officer at Hanwell Mental Hospital, an investigation regarding the blood pressure and Goetsch reaction in dementia praecox. The following is a summary of Dr. Dawson's results.

The Blood Pressure and Goetsch Reaction in Dementia Praecox.

In a series of 50 cases the blood pressure was as follows:

	No. of Cases.	Systolic Blood Pressure.		
		Average.	Minimum.	Maximum.
Katatonic	27	116 mm.	93 mm.	135 mm.
Simple dementia praecox ...	14	117 mm.	104 mm.	126 mm.
Paranoid dementia praecox ..	7	120 mm.	115 mm.	136 mm.
Hebephrenic dementia praecox	2	115 & 122		

The diastolic reading was between 55 and 65 mm. in all cases.

Goetsch Reaction.—A subcuticular injection of 0.05 c.cm. of 1 in 2,000 Parke, Davis and Co. adrenaline solution was made in all cases. Two cases only gave a normal reaction; these had a systolic blood pressure of 122 and 128 respectively. One was a katatonic and the other a simple dementia praecox case with congenital defect. Eighteen cases gave a moderate reaction: in 13 of these the blood pressure was 120 or under (minimum 104); in 5 it was over 120 (maximum 130). Thirty cases reacted only faintly: in 25 the blood pressure was 120 or under (minimum 98); in 5 it was over 120 (maximum 136).

The test was repeated in cases with a high blood pressure which gave a faint reaction, and the same result was obtained. In several cases it was found that a faint reaction might be intensified by administration of thyroid extract, but without material alteration in the blood pressure.

Katatonic Stupor.—Nine cases of this variety of dementia praecox were included in the series. One case had a blood pressure of 135, but reacted faintly to the Goetsch test. In the other 8 cases

* This research was carried out with the aid of a grant from the Board of Control.

† Dr. Langdon Brown, in his interesting Croonian Lectures on the sympathetic nervous system in disease, says: "It is both interesting and suggestive to note that an important group of endocrine glands—the adrenals, the thyroid, and the pituitary—have three features in common: the secretion of each is stimulated by the sympathetic, they all lower carbohydrate tolerance, and they all act and react with the reproductive organs."