

creased energy. There is no record of any influence having been exerted on the pulse and respiration.

**Therapeutics.**—The best results, it is claimed, are obtained in *neurasthenia*, but suggestion cannot be excluded. In *epilepsy* and in a case of *bulbar palsy* one authority reports excellent effects. In *mental diseases* the psychopathic disorders seem to remain unaffected, whereas the physical condition of the patients improved greatly under this treatment. Of eleven cases of *tubercles* treated with nervous extracts seven are reported benefited.

As against many favorable reports we find an equal or even greater number of absolutely negative results. Nerve-tissue extracts probably possess tonic properties for the nervous system and merit employment in this sense. Many other remedies that we possess are, however equally efficacious, so that nerve extracts are by no means an indispensable adjuvant to our therapeutic armamentarium. Charlatans in and out of the profession have utilized these preparations extensively to impose on a credulous laity, so that their employment has fallen into considerable disrepute among conservative physicians.

#### V. THE SECRETING GLANDS.

Aside from their external secretion some of the glands of the body seem to furnish an "internal secretion" that plays an important part in intracellular digestion. In the case of the pancreas and the kidneys this may be practically considered established; in the case of the liver, the intestinal glands, the mammaræ, and the salivary glands it is highly probable.

1. **THE PANCREAS.**—Complete extirpation of the pancreas is invariably followed by the complete syndrome of diabetes mellitus. If a small portion of the gland is left behind, or if a piece of the extirpated pancreas is subsequently grafted under the skin, diabetes does not develop. Ligation of the pancreatic duct does not cause diabetes. There are numerous theories in regard to the rôle of the pancreas in carbohydrate metabolism; they cannot all be discussed in this place. The preponderance of experimental evidence points to the secretion by the pancreas of a glycolytic, *i. e.*, dextrose-destroying ferment. If this secretion becomes insufficient or is arrested, the blood sugar is not destroyed, consequently it accumulates. This leads to hyperglycæmia and glycosuria. Diabetes may also be due to other causes. Degeneration of the pancreas in man may and may not produce diabetes. From very recent investigations it appears that in nearly all cases of diabetes certain cell groups in the pancreas (the "islands of Langerhans") are found degenerated. These cells are not connected with the efferent ducts of the gland, but pour their secretion into the lymph spaces. It is probable that they furnish the specific internal secretion. Ligation of the pancreatic duct causes atrophy of the cells furnishing the external secretion, whereas the islands of Langerhans remain intact for a long time. The writer is at present engaged in studying the effects of pancreas prepared in this way, *i. e.*, of "isolated" islands of Langerhans in carbohydrate metabolism, both *in vitro* and *in vivo*. It is expected that these researches will throw light on the nature of the internal pancreatic secretion, and will advance the organotherapy of diabetes. For the present this method of treatment, although so clearly indicated on theoretical grounds, has furnished essentially negative results. This may be due to the fact that all pancreatic extracts contain digestive ferments and certain nucleoproteids that are toxic and produce local necrosis when injected hypodermically; thromboses, pyrexia, tachycardia, increased diuresis, and increased N-excretion when administered intravenously. The administration by mouth is negative in diabetes. It is probable that the trypsin contained in pancreas extracts destroys the "internal secretion" as it destroys the fat-splitting enzyme that we know to be present. An extract of pancreas containing no digestive ferments, prepared as suggested above, may act more favorably.

The administration of pancreas by mouth is practised

for the relief of *steatorrhœa* and other *intestinal disorders* that are due to perversion or absence of the external secretion of the gland. This treatment is not, however, organotherapy proper, and will therefore be discussed under other headings.

2. **THE KIDNEYS.**—Complete anuria may persist for many days without causing the development of uræmic symptoms (*e. g.*, hysterical anuria). If a double nephrectomy is performed in a dog and kidney extract is injected intravenously, the life of the animal will be prolonged beyond that of a nephrectomized control animal that is not treated with renal extract. The onset of uræmic symptoms can be delayed in this way. From these observations the conclusion has been drawn that the kidneys furnish an internal secretion that is disintoxicating for certain urinary bodies, and that prevents the occurrence of uræmia. It has also been shown that the toxicity of the blood of uræmic animals is greatly reduced by its passage through healthy kidneys. Uræmia is not, therefore, considered to be due to the retention of urinary bodies alone, but also to insufficiency of the internal disintoxicating secretion of the kidneys. In harmony with this theory kidney extract has been employed in the treatment of a considerable number of uræmic cases, apparently with good results. Kidney therapy is too modern, and case reports are too scanty to warrant extended analysis. The subject, however, seems capable of fruitful development.

3. **THE LIVER.**—Liver extract contains many substances with active physiologic and toxic properties, and no less than ten well characterized ferments besides. It is difficult therefore to understand how those who employ liver extract for the sake of an hypothetical internal secretion of the hepatic cells can exclude the action of all these bodies. It has been claimed that the virtues of cod-liver oil are due to the presence in this product of an internal secretion. A few good results are reported from the use of hepatic extract (prepared according to d'Arsonval's method) in *diabetes*. The preparation is said to stimulate the liver cells to increased activity in the sense that it enables them to store more glycogen. A great reduction in the sugar excretion has been reported by reliable clinicians. Some authors have also used liver extract symptomatically for "*hepatic insufficiency*" following alcoholic cirrhosis, and report improvement of many of the subjective symptoms.

4. **MAMMARY GLAND.**—Mammary gland extracts are believed to exercise an influence on the female generative organs. Desiccated sheep's mamma has been given by mouth in twenty-grain doses for *uterine hemorrhages*. It is said to cause contraction of the uterine muscles and to arrest bleeding. Good results are also claimed from this therapy in the leucorrhœa and irregular bleeding of sub-involution, and in benign tumors of the uterus it is said to relieve many of the reflex symptoms, to control the leucorrhœa and bleeding, and to improve the general health of the patient.

5. **INTESTINE.**—There is some experimental evidence to show that the intestinal wall neutralizes many of the toxic products that are generated in the bowel lumen. Insufficiency of this function would lead to autochthonous intestinal intoxication. It has also been shown that the injection of sterile feces does not produce death so rapidly in animals which have been treated with intestinal extract as in animals which have not. The disintoxicating action of the cells of the intestinal wall is believed to be carried out with the aid of a soluble internal secretion which they produce. It does not seem improbable that the violent systemic disturbances of intestinal strangulation, volvulus, and invagination are in part due to insufficiency of this function and the resulting self-intoxication. The same applies to certain anæmias, psychoses, etc., which may be attributed to auto-intoxication from the bowel.

Extract of intestine has, in fact, been employed with some success in *chlorosis*, and in several cases of stercoræmic poisoning following *strangulation* of intestinal hernias. We are told that in a few of the latter cases the general condition of the patients improved so much un-

der this treatment that operative interference was rendered more safe. This field of organotherapy also merits further cultivation.

6. **PAROTID GLAND.**—The parotid gland and the ovaries appear to stand in some sympathetic relation to one another. Parotid extract has been used with success by eminent clinicians in Germany and Scotland for the relief of certain symptoms due to ovarian disorders, notably the pain and reflex manifestations of ovaritis in cases in which the glands were enlarged and prolapsed.

#### VI. MISCELLANEOUS TISSUES.

Nearly every tissue of the body has at some time been made to yield an extract. No exhaustive experimental or clinical data relating to their employment are, however, recorded excepting in the case of muscle tissue, lung tissue, and heart. We will therefore discuss these three alone.

1. **MUSCLE TISSUE.**—Muscle extracts contain abundant quantities of potassium salts and consequently are toxic when given hypodermically. In addition, muscle juice has a distinct thermogenic action and can produce salivation. Reliable investigators claim that small quantities of muscle extract prepared in the cold and sterilized under CO<sub>2</sub> pressure act as distinct muscle tonics.

Muscle extract has been employed apparently with some success in all primary myopathies in which there was no injury to the anterior horns or the peripheral nerves. A leading French neurologist recommends its use in all "*dystrophies musculaires progressives*" with lesions of the fibrillæ of the muscle and connective tissue.

2. **LUNG TISSUE.**—Pulmonary extract has been successfully employed in the treatment of pulmonary arthropathies. It is believed that destructive lesions of the lungs, in addition to interfering with the respiratory interchange of gases, inhibit the formation of an internal secretion of the pulmonary cells, and that the lack of this secretion in the blood leads to the development of the osteo-arthritis lesions of lung disease. Very good results are reported from pulmonary therapy in a case of Marie's disease (*ostéo-arthropathie hypertrophique pneumonique*). The arthritic process was arrested, the dynamometric pressure rose from 9 kgm. to 19.5 kym., and the general health of the patient was markedly improved after the twenty-ninth injection. In pleuro-pulmonary suppuration with osteo-arthritis pulmonary extract is also said to act beneficially, and recently "pulmozyme," a pulmonary preparation, has been advised for the treatment of lesions of the lungs themselves. Case reports are scanty and results not uniform, so that judgment cannot as yet be rendered on this therapy.

3. **HEART.**—Heart extract was extensively used a few years ago in the treatment of a large variety of disorders. The effects claimed from the injection of this preparation were, among others, an increase in the pulse rate, a rise of arterial pressure, increased diuresis, and a general tonic effect. The extract used by the chief advocate of cardiotherapy unfortunately contained appreciable quantities of alcohol, so that we need not be surprised to learn that it exercised the above effects. The literature on cardiotherapy is large and many cures are reported. A careful analysis of the case reports, however, reveals the method to be utterly devoid of value and the claims of its advocates to be unfounded. Cardiotherapy is mentioned only to be condemned. *Alfred C. Croftan.*

**ORPHOL.** See *Naphtol-bismuth*.

**ORRIS ROOT.**—(*Rhizoma Iridis*, Ph. G.; *Iris de Florence*, Codex Med.) The peeled rhizomes of three or more species of *Iris* are cultivated for this object in the south of Europe, especially in the vicinity of Florence. They, and a few other species also, are familiar garden flowers both there and in this country. The three following are recognized as the sources of "Orris": *I. florentina* L., with very sweet-scented, white, or pale slaty-blue flowers; *I. germanica* L., with dark, violet flowers; and *I. pallida*

VOL. VI.—27

Lam., with flowers light blue, very large, and fragrant. They all resemble each other in respect to the more important particulars. The former is a native of the southern and eastern Black Sea regions, the others of Europe; all have been cultivated for a long time.

The rhizomes are gathered in the latter part of summer, trimmed and peeled, and then dried in the sun, and afterward separated into grades, according to size, symmetry, and appearance. The pieces are more or less long and flattened, with rounded surfaces and ends, often curved or twisted in drying, of a nearly white color, a hard but brittle texture, and a yellowish fracture. Pieces with the branches attached are called "hands"; the detached branches, "fingers." The scars where the roots have been cut away may be seen on the lower surface. Taste bitterish, aromatic, and sharp. Odor, for which it is valued, mild and pleasant, recalling that of violets. Orris which has been kept for one or two years is more fragrant than that just dried. This product has been for centuries used as a perfume, and less generally as a medicine, and is mentioned by most of the classical writers upon medicine. It yields, upon distillation, about 0.1 per cent. of a so-called volatile oil, "*orris camphor*," a buttery-looking substance. This consists chiefly of *myristic acid*, with a trace of *irone*, a liquid with a violet-like odor. *Iridin* is a glucoside, occurring in acicular crystals, in very small amount. There is a specific amaroïd, giving the bitter taste. Orris contains also a little resin and fixed oil, and a very little tannin. Starch is abundant.

**ACTION AND USE.**—Internally given, orris, like our Blue Flag (*Iris versicolor* L.), is a cathartic and occasional emetic, but it is almost never employed in this way. It is a common ingredient of tooth powders, as well as of sachet powders (violet), and is otherwise used as a perfume. The oil is also used in tooth washes. Large, fine pieces are now and then given to teething children to chew upon. *Henry H. Rusby.*

**ORTHIN.**—This is one of the numerous compounds introduced for its antipyretic properties. It is a combination of hydrazin and para-oxybenzoic acid; the base is an unstable body, but the hydrochlorate is a stable preparation, and is the salt supplied under the name of orthin. It is very soluble in water. The solution should always be freshly prepared and preserved from the light. It is recommended as an antipyretic in typhoid fever, pneumonia, rheumatism, and all febrile disorders. Kobert, who introduced it into therapeutics (*Deutsche med. Wochen.*, 1890), claimed that it was non-toxic and free from all ill effects. Its use, however, has been accompanied by sweating, prostration, and other symptoms of poisoning. The dose advised by Kobert is from five to eight grains. *Beavmont Small.*

**ORTHOFORM**—meta-amido-para-oxybenzoic methyl ester (C<sub>6</sub>H<sub>5</sub>.OH.NH<sub>2</sub>.COOCH<sub>3</sub>)—is a white powder without odor or taste, and permanent in the air. It is soluble in alcohol, ether, chloroform, and some of the oils, but very slightly soluble in glycerin or water. It is precipitated, but not rendered inert, by formaldehyde and mercuric bichloride (Luxenburger), produces a brown color with bismuth subnitrate, and decomposes silver nitrate and potassium permanganate. It is not affected by zinc oxide, iodoform, salicylic acid, carbolic acid, lysol, aluminum acetate, or iodine, and may be safely combined in prescription with most of the ordinary antiseptics and dusting powders. It is said to remove most of the odor of an equal amount of iodoform.

Acting on the sensory end-organs, orthoform produces a local anesthesia, which, owing to the insolubility of the drug, is mild and long continued. This slow action, together with a distinctly antiseptic power, makes it a valuable dusting powder for raw surfaces. It is therefore applied to burns, fissures, painful ulcers, ulcerating hemorrhoids, etc. The anaesthetic effect from a ten-per-cent. powder or ointment lasts for from two to forty-eight hours (Kindler). As the drug has no penetrating power,



it is of little use on unbroken skin or mucous membrane. Blondel used a few drops of a saturated solution in forty-per-cent. alcohol for fissured nipples. In zoster or herpes with ruptured vesicles much relief is obtained.

In throat and nose work its use is chiefly limited to ulcerative conditions, though Cheatham reports good results in rose fever. Garnaud's formula for laryngeal tuberculosis is: Menthol 3.0 (gr. xlv.), cocaine alkaloid 0.5 (gr. viij.), orthoform 2.7 (gr. xl.), expressed oil of almonds, 100 (℥ ij. ʒ ij.). It is also used as a spray in five-per-cent. solution in alboline. In painful cancer and ulcer of the stomach it has been administered in dose of 0.5 (gr. viiss.) several times a day with relief from the pain and without any systemic effect. Suspended in water it has been thrown into the bladder for painful cystitis. In dentistry, its slow anaesthesia fits it for allaying the ache of an exposed nerve.

Orthoform is used in five to twenty per cent. powder, ointment, collodion, or solution in oil. Injected hypodermically in alcoholic solution it acts like cocaine, but the latter drug is generally preferred.

Ruhemann, H. H. Wilson, Vogt, Decker, and others who have extensively employed the drug, report the occasional occurrence, from its use, of a peculiar vesicular dermatitis resembling that from poison ivy and very resistant to treatment. Brocq observed hyperæmia and pruritus. Miodowsky had a moist gangrene following the application of a five-per-cent. ointment, and Friedländer collected fifty cases of local or general poisoning and eczema.

W. A. Bastedo.

**ORTHOFORM, POISONING BY.** See *Synthetic Poisons, Organic*.

**OSMIC ACID.**—In medical parlance the title *osmic acid* is given to the body *osmic tetroxide*, OsO<sub>4</sub>. True osmic acid (H<sub>2</sub>OsO<sub>4</sub>) is not known in the free state. Osmic tetroxide is a volatile crystalline substance, softening at a moderate heat like wax, and melting at a lower temperature than does that body. It dissolves slowly but completely in water, forming a colorless solution, which, however, on exposure to light, rapidly darkens, even to blackness, by decomposition of the tetroxide with formation of the tetrahydroxide, Os(OH)<sub>4</sub>. Osmic tetroxide is a powerful oxidizer, and, to living tissues, is excessively irritant. Its odor is powerful and disagreeable, and its vapor intolerably pungent and poisonous, with a peculiar faculty for exciting irritation of the conjunctiva. In the event of the inhalation of fumes of osmic tetroxide, hydrogen sulphide ("sulphuretted hydrogen") has been recommended as a chemical antidote, to be taken by inhalation; but since in this case the remedy is itself a powerful poison, the greatest care would be required in its employment.

Osmic tetroxide is of peculiar service to the histologist, by reason of a faculty it possesses of staining nerve tissue. As a medicine it has been used, by hypodermic injection, for the relief of peripheral neuralgias. The results have been quite variable, but a certain amount of efficacy for the remedy seems to have been demonstrated. A one-per-cent. aqueous solution of the tetroxide is used, and the same should be made only in small quantities when wanted, and kept in the dark. Of such a solution, quantities from 0.20 to 1 gm. (from ℥ iij. to ℥ xv.) have been injected at a dose. The injections are made as near as possible to the painful spot. The operation is often severely painful, is occasionally followed by temporary swelling and thickening of the tissues at the site of the puncture, and, practised over an efferent nerve, has in one instance been followed also by paralysis. No constitutional effects have followed these injections.

Edward Curtis.

**OSPEDALETTI, ITALY,** a town of one thousand inhabitants, with nearly a mile of frontage toward the sea, is situated midway between Bordighera and San Remo. It is a quiet Riviera resort, lying under the spurs of the Ligurian Alps, well sheltered from the winds and with a south-

ern exposure. "There is no doubt," says Dr. Wendt, in an article upon this resort in the previous edition of the HANDBOOK, "that little Ospedaletti is more effectually protected from winds than almost any other resort on this coast. Moreover, it gets the sun early and keeps it late. There is less blinding calcareous dust there than, for example, at Hyères, Cannes, or Nice."

"Ospedaletti spreads out for something like a mile along the head of a small crescentic bay. The eastern headland of this bay is formed by Cape Nero, and the western extremity, much farther from the village than the former, by Cape Sant Ampeglio. Thickly planted with olive hills surround the place, relieved in the plain by orange and lemon trees, and the usual array of graceful palms. Successive girdles of mountains protect it from the icy north blasts, but less in a northeasterly than in a northwesterly direction. It is fully exposed only to the warm westerly marine breezes." "Immediately behind this village there rises a hill of gentle slope, and a number of mountain torrents of mild proportions trace their undulating course seaward." "The place is so hedged in as to constitute a veritable sun trap." "For undergoing a course of absolute quiet and repose," continues Wendt, "in a sunny, well protected situation, no more suitable place has yet come to my notice on the Riviera."

The hygienic conditions of Ospedaletti appear to be good; the town is spoken of by Linn as having a particularly clean and neat appearance. The drinking-water comes from the same mountain source as that which supplies San Remo, and is "soft, sparkling, and pure." The mean temperature of five winters is given by Linn ("The Health Resorts of Europe," by Thomas Linn, M.D., 1901) as follows: January, 49.82° F.; February, 51.62° F.; March, 53.42° F. The mean relative humidity is 62 per cent., and the number of rainy days, 32.

There are several hotels and pensions of moderate price, well kept, and very comfortable. There is also a fine casino. Medical service can be had there. A short distance from the village are some hot sulphur springs. "Gouty and rheumatic elderly people," says Wendt, "should do particularly well at Ospedaletti." Linn states that this place is rapidly coming into favor as a resort, and it seems to combine very many favorable conditions for a winter health station, viz., its fine natural situation, its pleasant surroundings, its excellent protection from cold winds, the large amount of sunshine, its near proximity to San Remo and Bordighera, and the quiet and repose obtainable there. Moreover, it is said to be two degrees warmer than its neighbors, Bordighera and San Remo.

Edward O. Otis.

#### OSTEITIS, OSTEOMYELITIS, PERIOSTITIS.

**I. OSTEITIS.**—Inflammation of bone may be induced by simple traumatism—as a fracture or stripping away the periosteum, by thrombosis or embolism of a nutrient artery, by extension from a periostitis, by extension from arthritis, by exposure to cold or to the action of certain poisons—as phosphorus and mercury, by syphilis, by pressure—as the rarefying osteitis of aneurism, by the eruptive fevers, and especially by typhoid fever. While these fevers may possibly act as primary causes, it is quite certain that they predispose to the development of an osteitis. Lastly, certain germs play an important part in the causation of an osteitis. They are either introduced through compound injuries, or else they are carried to the bones by way of the circulation. The emphasis which should be laid upon this last factor in the causation of osteitis cannot be exaggerated.

It is of little clinical value to classify the inflammations of bone, from an anatomical standpoint, into osteitis, osteomyelitis, and periostitis, since primary periostitis, with the exception of the traumatic and the syphilitic varieties, is very rarely observed; and, on the other hand, every case of myelitis leads, sooner or later, either rapidly or slowly, to involvement of the periosteum in the inflammatory process.

Regarding the firm bony substance itself, when compared with the marrow and the periosteum, it may be

truly said not to take any active part in inflammation; and therefore osteitis, in a narrower sense of the word, as compared with myelitis and periostitis, is unimportant. The firm bone, however, is passively affected, as we shall subsequently notice; and clinically the death of the bone, or of a part of it, may prove to be an affair of the greatest gravity. So much is this true that it has been customary to study acute osteitis under the title of one of its most frequent results—necrosis—and a certain form of chronic osteitis under the heading of caries.

**II. PERIOSTITIS.**—Periostitis, like osteomyelitis, may originate from traumatism, either simple or compound, and in character may be simple (that is, aseptic) or septic (from the presence of micro-organisms). The syphilitic variety of the disease should probably be classed under this latter heading, although we cannot to-day speak with certainty as to its germ origin. The periosteum is first affected during the secondary stage of syphilis, that is, the stage of invasion following the incubation of the syphilitic virus in the system. Those bones which are subcutaneous seem especially liable to periostitis—for example, the tibia, sternum, and ulna; but the others are not exempt. In severe cases there sometimes appears to be a simultaneous involvement of most of the bony sheaths of the body, with consequent almost unbearable osteoepic pains. These pains are distinctly worse at night, and seem to be increased by warmth; but I am inclined to think that sufferers from osteitis and periostitis of other than syphilitic origin also complain most at night.

The syphilitic periosteum is quite tender, and I have many times noticed pitting on pressure. In this disease it is rare for the periosteum to become separated from the bone by exudations; and consequently necrosis, from failure of the superficial blood supply, is very infrequent in this form of periostitis.

In the later or "tertiary" stages of syphilis, nodes, usually flat, and of sharply defined extent, sometimes make their appearance. They are caused by infiltration of the periosteum with small round cells, and, like all gummata, tend to soften and break down. Their course, and the probability of bone involvement, seem influenced for the worse if the medical attendant, finding fluctuation, use the knife instead of rapidly pushing the iodides or other appropriate medicines.

In acute periostitis, when accompanied by free exudation of fibrin, serum, and pus, the cortical lamellæ of the Haversian systems may be separated from their vascular supply; and unless the surgeon promptly realizes the state of affairs, and makes free incisions down through the dense, unyielding periosteum to the bone, a necrosis of more or less superficial character may, and often does, result.

The clinical picture of acute periostitis is best studied, as it will be later, together with osteomyelitis; for these two diseases are commonly associated together.

A rather rare concomitant of an acute osteomyelitis, usually of a mild type, is a periostitis with exudation of a simple serous character between the periosteal sheath and the bone. Because of the abundance of albumin in this fluid, Ollier here adopted the title of "osteitis albuminosa."

Chronic, non-infective periostitis may be either fibrous or ossifying in character. In the former there is much increase in the amount of connective tissue, and the thickened membrane adheres unusually closely to the bone. In the latter we have as a result an ossific deposit, which may go on increasing for months or even years, ultimately producing exostoses or osteophytes. The new bone of inflammatory origin is not deposited in a regular system of lamellæ, probably owing to faulty nutrition; and it is sometimes absorbed, and disappears, the abnormal activity of the osteoblasts ceasing. This variety—ossifying periostitis—may be associated with either rarefying or condensing osteitis.

With regard to tuberculous periostitis I may state that it is especially apt to appear in the subjects of the so-called scrofulous diathesis, and in the poorly nour-

ished, and to be accompanied by tuberculous osteitis. The discussion of its symptoms, course, and treatment need not be dissociated from that of the latter disease.

**III. OSTEOMYELITIS.**—The terms osteitis and osteomyelitis will here be considered as one. Where the vascular changes greatly predominate, where pus, fibrin, and serum are abundantly produced, where the brunt of the inflammation is felt by the marrow and contents of the Haversian spaces, the latter term may be applied with especial propriety. And, on the other hand, those cases in which changes in the firm bony structure itself form the prominent feature, may properly be designated as cases of osteitis. However, the two go hand-in-hand. Changes in the relative density of the bony structure can occur only through cellular activity in the marrow spaces and vascular canals. These changes are of two kinds: osteoporosis, or rarefying osteitis, and osteosclerosis, or condensing osteitis. In the former the character of the bone changes from compact to cancellous, and if the process continue the bone may even entirely disappear, its place being taken by a mass of granulation tissue. This variety of osteitis is very common. It is one of the essential phenomena in tuberculous osteitis; it is the process by which the rough, ossified callus following fractures is rounded off; and when a bone is subjected to pressure—as by a growing aneurism—it is a rarefying osteitis by which it is eroded.

In osteosclerosis, on the other hand, the bone grows more compact, and may even—as may be observed in some exostoses—become as dense as ivory.

It often happens that both osteoporosis and osteosclerosis are going on at one and the same time in different parts of the same bone: an osteoporosis within, for example, and an ossifying, even condensing, periostitis externally; and as a result the bone may become widely expanded, although it is a mere shell filled with granulations or with inflammatory deposits.

Or, again, following an osteoporosis, the opposite process may be inaugurated, and the cavities caused by the former morbid process may become filled with new bony deposit, perhaps of even abnormal density. We do not yet know why inflammation of bone terminates sometimes in one and sometimes in the other of these conditions. It is supposable that in condensing osteitis the osteoblasts have an undue activity. In rarefying osteitis the absorption of bone is thought by some pathologists to be caused by the presence of certain large, multinucleated cells—the myeloplaxæ of Robin; cells which are also by reason of the power which they are supposed to possess, called osteoclasts. In subacute osteomyelitis ragged holes, opening from the marrow spaces and Haversian canals, are formed in the solid bone. These cavities are known as the caverns or lacunæ of Howship. They contain many of the so-called osteoclasts, which, if not the cause, are certainly the witnesses of the osteoporosis.

Other pathologists repudiate the idea that these large cells possess any such power, and attribute the absorption to the influence of the new granulation tissue which is present in these cases, and which lies in contact with the bone. In agreement with Billroth they hold that just as a granulating synovial fringe erodes the articular cartilage against which it rests, "like ivy climbing over a ruin," so here in bone the granulations possess a similar disintegrating power.

In acute osteomyelitis the vascular changes are of the deepest import, since obstruction of the nutrient arteries means death of the bone *en masse*. Let us study the common cases of apparently spontaneous origin. Here the marrow tissue is at first of a deeper red, from intense congestion. Sometimes it is mottled with hemorrhagic spots. Later, a grayish hue appears, due to the presence of great numbers of pus cells; and occasionally little-medullary abscesses develop. In bad cases not only does thrombosis of the nutrient vessels occur, but gangrene of the marrow and of the contents of the Haversian canals also takes place, with rapid liquefaction. The bone cells being no longer nourished die. The infection may spread rapidly, involving the whole length of the bone,