that he was unable to find in the literature at his command a single instance of researches of this character, and he adds that Ziegler also knew of none. Reinbach prefers to abandon the older nomenclature comprising such terms as fungous, spongy, erethistic, croupous, etc., for the general term pathological granulations.

Of these he recognizes two forms with several subordinate types: (1) The *luxuriant superficial granulation*,

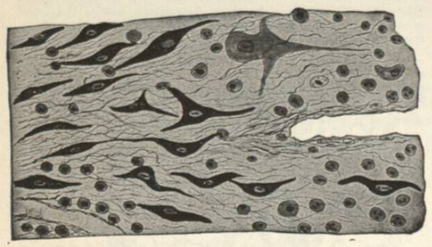

FIG. 2348.—Organizing Granulation Tissue. The left edge represents the deeper part. The round cells are both mono- and polymorphonuclear leucocytes. There are many spindle-shaped fibroblasts. (Modified from Ribbert.)

that is usually "self-purifying" and characteristic of acute processes, and (2) the *superficial chronic granulation*. The strictly torpid granulations he classifies with ulcers on account of the absence of formative tissue. As for the first form they are marked by the histologic features that belong to the process of suppuration (see *Inflammation*). Quantities of bacteria occur—generally cocci that show no special arrangement—and at different levels the changes indicative of miliary or microscopic abscesses. Leucocytes swarm within such granulations, and among them eosinophiles and mononuclear leucocytes are numerous. The capillary loops of the outer zones suffer some necrosis. In spite of the exudative and destructive changes karyokinetic figures are numerous in the deeper portions in fibroblasts and endothelial cells, and the fibroblasts produce fibres and become connected in the usual way.

As examples of superficial chronic granulations, Reinbach mentions both the torpid granulations, which, however, show some signs of growth, and those covered with mottled and white patches caused by necrosis of the outermost parts. The first of these subdivisions, although very slow to heal, nevertheless contain vertical bands of fibre-forming cells. They often follow burns and constitute virtually lesions intermediate between granulation tissue and real ulcers. The second variety, covered by a fibrinous exudate in spots and by necrotic tissue, was described by Billroth as "croup of the granulations." Surgeons on meeting with these hindrances to the normal course of healing are inclined to suspect wound diphtheria, *i.e.*, a true infection with the bacillus of diphtheria. However, such areas of necrosis superficially located upon otherwise healthy granulations may be caused by other non-pyogenic bacteria, for example, the Bacillus coli.

The fibrin upon these diseased granulations, commonly limited to the periphery, may extend to considerable depths; when the spots clinically are dark yellow and brown, the necrosis may be accompanied by practically no inflammatory changes.

A careful review of the work of Reinbach demonstrates quite clearly that the interferences with the process of cicatrization in granulation tissue are due to the precipitation of fibrin either as a covering or among the cells, to simple necrosis, or to that form of necrosis which with serous exudation or liquefaction is generally known as suppuration. His work is based upon the careful histologic examination of tissue removed from many conditions that were associated with granulating surfaces. There is urgent need of equally thorough bacteriologic examination of such diseased human granulation tissue, especially researches that would include the use of animals.

There is yet another fact that prevents normal cicatrization, and that is obstruction to the blood supply of the growing tissue. The obstruction is only partial, and without doubt in many instances is attributable to an arterial supply that is inadequate in the number of vessels or their total calibre. In other cases the action of morbid conditions more centrally located or dependency of the part leads to inefficient supply of blood. That an œdema of granulation tissue may occur is well known; doubtless a deficiency in quality or quantity of nourishment is responsible for the occasional total failure of resolution. Briefly, granulation tissue may be the seat of extensive necrosis, œdema, and suppurative or fibrinous inflammations as well as combinations of these processes. Other pathological conditions, such as hemorrhage and the various cellular degenerations, may arise, but generally only as minor and incidental changes. The causes of pathological granulations often are to be sought in the character of the primary lesion, rather than in secondary infection or the injury of healthy granulations. Infection at the time of injury is frequently responsible for subsequent difficulties in healing.

THE PROTECTIVE QUALITIES OF GRANULATION TISSUE.—It is well known that granulations bleed readily; slight trauma of any sort disturbs the unorganized tissue and lacerates the embryonal and sprouting capillaries. As for infection, many experiments have proven that in this respect granulation tissue constitutes a serviceable barrier. One of these was the now classical experiment of Billroth. He ascertained that no ill effects followed daily dressing of healthy and experimentally produced granulations of a dog's back with lint saturated with pus, whereas inoculating such animals with the same material caused death. This simple test was many years later followed by the extensive experimental study of Afanassieff, who in a more scientific manner and by exact bacteriologic technique verified the results of Billroth.

Granulations were produced upon many animals of different species, and upon them virulent cultures of such bacteria as the bacillus of anthrax and the vibrio Metschnikovi were carefully smeared with a thick platinum needle. The serum exuding from granulations so treated was examined from time to time, stained preparations and media inoculations being made also; the virulence

FIG. 2349.—Perivascular Collection of Round Cells or So-called Lymphoid Tissue. They contain various forms of leucocytes, and as the inflammation becomes chronic, plasma cells occur in such cell accumulations. (Modified from Ribbert.)

of the resulting growths was examined; histologic examination of the granulation tissue for bacteria and the inflammatory changes was carried out, and animals were killed in order to ascertain if general infection had occurred. Ample control experiments were employed.

He found that bacteria placed upon healthy granulations of animals did not penetrate, nor did general infection result. Inoculations made with recovered growths of the bacteria denoted an attenuation in virulence by the sojourn upon granulation tissue. Afanassieff was strongly inclined to look upon the protection afforded by the granulation tissue in the light of a vaccination. Such an explanation, however, is controverted by two facts. One of these is that local reactions in the granulation tissue were not observed with sufficient regularity in all animals to be in accord with the production of a bacterial immunity. Another fact is that Noetzel has repeated many of the experiments of Afanassieff and found that after bacteria were kept in contact with granulating wounds for many days the animals did not acquire any immunity.

It must be remembered that in granulation tissue mechanical obstacles exist to infection, such as the outward current of fluid from the vessels and the exceedingly slow circulation. Phagocytosis undoubtedly plays some part, although it may be that the ingested bacteria are no longer viable at the time of their incorporation. The extracellular destruction of the bacteria by the fluids present in granulation tissue (Afanassieff) or by enzymes, belongs to fundamental problems of immunity (see *Immunity*).

One cannot overlook the fact that when granulation tissue has formed, a defensive mechanism has been produced and its production is in response to external injury. But granulation tissue usually contains bacteria; especially frequent are the ordinary pyogenic forms.

Although resistant to bacterial infection, granulating wounds allow of the ready absorption of many soluble substances. Roux, Bonnet, Demarquay, Gorny, Maas, and Hack, and many others, have made experiments regarding this. Not all substances are absorbed with equal facility. The concentration of the solution, its chemical composition, the size of the granulating surface, and the character of the injury producing it, as well as the time contact is allowed, all influence the absorption. Granulating surfaces following burns and caustics are not so permeable as some others; absorption is more rapid from some healing wounds than from freshly cut surfaces. Apomorphine and curare are not readily absorbed, but carbolic acid diffuses with great facility. Various alkaloids such as strychnine, morphine, pilocarpine, cocaine, etc., have been used, and carmine, sodium sulpho-indigotate, iodoform, potassium iodide, sodium salicylate, as well as many other substances. Hack recovered ferrocyanide of potassium from the urine ten minutes after its application to a granulating surface, and Maas was able by spraying abscess cavities with a camphor solution, in a patient with vertebral caries and pyæmia, to sustain the heart action sufficiently to allow operation. These and many other interesting and curious facts have been discovered about this phase of granulation tissue.

CICATRIZATION.—With healing of wounds by granulation a scar is formed that becomes paler as contraction takes place. Resolution in this form of inflammation is not marked by any peculiarities that distinguish it from cicatrization elsewhere. It is, however, customary to refer in this connection to the very deforming contractions that sometimes follow burns, but it is the location of the cicatrix rather than any special properties it possesses that marks it as singular. The loose subcutaneous adipose and areolar tissues allow scars to produce disfigurements that excite special interest on account of their exteriority. Similar malformations may occur in less exposed locations that are fully as interesting and as remarkable—for instance, the acquired dextrocardia and lesser dislocations of the heart that follow indurative processes of the neighboring viscera. They constitute excellent examples of the partial failure of inflammation as an adaptive process. The development of keloids in scars might be cited as another instance in which abnormal resolution builds a growth, which, to the surgeon at least, must ever serve as a striking illustration of the failure of inflammation as an adaptive process. In contrast to these irregularities in resolution and fully as interesting is the failure of granulation tissue to organize about certain fistulous passages and their openings that lead to foreign bodies, necrotic tissue, etc. These are the so-called "sequestrum granulations." The failure of cicatrization in these cases seems to indicate a better adaptation of the process of inflammation, as it occurs in granulation tissue, to meet the requirements.

E. R. Le Count.

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GRAPE.—(Including *Raisin*, or *Uva Passa*.) The genus *Vitis* Tourn. (fam. *Vitaceæ*) comprises about thirty species of Vine, a number of which, either in their improved forms, or as hybrids, contribute our grapes. The young leaves, tendrils, and green fruit of the vine are sour and astringent, containing *tartaric*, *malic*, and other fruit *acids* or their salts; *tannic acid*, *quercetin*, *quercitrin*, etc., sugar, gum, and several earthy and alkaline bases. They are more or less employed in Europe in the form of "teas" or syrups as domestic remedies. The juice of one particularly sour variety expressed from the green fruit, and known as *verjus*, is used to make a flavoring and refreshing syrup. The sap of the stems has also been employed. Ripe grapes, and especially raisins, are much sweeter, containing from ten to forty per cent. of *sugars* (*dextrose*, *levulose*, *inosite*) besides the acids, salts, etc., above mentioned. Still these are more or less employed for the same purposes as the herbage. Their medicinal virtues are very unimportant.

From the ripe fruit of the European Vine, *Vitis vinifera* L., raisins, and from one of its varieties the Greek, Zante or English "currants" are made merely by careful drying. Raisins are slightly laxative, like figs and other dried sweet fruits, and they have a peculiar power in imparting flavor.

Henry H. Rusby.

GRASSE, FRANCE, a town of 15,000 inhabitants, is eleven miles north of Cannes, from which it is reached by railway in forty minutes, and also by direct railway from Nice. This resort of the Riviera was brought especially to public notice by the visit of the Queen of England in the spring of 1891. It is very picturesquely situated, high above the hillsides, and is well sheltered from the cold winds on the north. It has an elevation of 1,070 feet, and possesses a very mild and salubrious climate, essentially the same as that of Cannes, with the exception that it is less stimulating than a resort directly upon the seashore.

The temperature is a little lower in winter than that at Cannes, on account of the elevation; the mean temperature of the year being 60.2° and for the winter 46.4°, while that at Cannes is 60° and 47.75° F. respectively. "Grasse," say Weber and Foster (Albutt's "System of Medicine," 1896), "forms a useful intermediate station during April and May for patients who find the heat in those months already too oppressive at Cannes."

For the climatic detail one is referred to the articles upon Cannes and Nice. In brief, Grasse affords a favorable winter resort for invalids unable to remain near the sea. Grasse possesses a luxuriant vegetation and is celebrated for the cultivation of flowers and the manufacture of perfume, which is the most extensive in France, if not in the world. The air is heavy with the scent of flowers, which with some invalids is said to produce an exaggerated form of hay fever. Great fields of orange blossoms, heliotrope, hyacinthe, roses, violets, jonquils, geranium, and other flowers are cultivated about Cannes and Grasse; 60,000 acres being devoted to this industry, yielding an-

nually 2,200,000 pounds of roses and 4,000,000 pounds of orange flowers.

At the foot of the village are great plains of olive trees. The views are very beautiful and extensive, and the excursions round about are many and attractive. The town itself is not particularly attractive, but this is compensated for by its picturesque situation and beautiful views.

The water supply is good, but the sanitary condition was said by Linn ("Health Resorts of Europe"), in 1893, to be far from perfect. The accommodations are good but apparently limited.

The climate is said to be beneficial to sufferers from asthma, gout, nervous affections, insomnia, neuralgia, and rheumatism. *Edward O. Otis.*

GRAVEL. See *Kidney Diseases.*

GRAVES' DISEASE. See the APPENDIX.

GREAT BEAR SPRING.—Oswego County, New York. This spring is located near Fulton. It has been known for many years, having been used by the aborigines. Within the last few years the spring has been improved and the water has an extensive sale in Syracuse. More recently it has been introduced into New York and other large cities. The water is but feebly mineralized, but it is remarkably pure, and its freedom from organic matter gives it excellent qualities for the table. Its very small cost is an additional advantage. The following analysis was made in 1890 by Dr. William Manlius Smith, of Syracuse:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Calcium sulphate	0.72
Calcium carbonate	3.50
Magnesium carbonate	1.25
Magnesium chloride	.47
Sodium and potassium carbonates	Traces.
Total	5.94

James K. Crook.

GREEN LAWN SPRING. Jefferson County, Illinois.

POST-OFFICE.—Mt. Vernon. Hotels and boarding-houses. These springs are located in the city of Mt. Vernon, 76 miles east of St. Louis. This point is reached by the Louisville, Evansville and St. Louis, by the Jacksonville and Southeastern, and by the Louisville and Nashville railroads. The springs are six in number, and are surrounded by a park of about eight acres in extent in the centre of the city. Their waters are discharged from a vertical stratum of slate about eight inches in width and bisecting a horizontal stratum of slate of between two and three feet in thickness. They belong to the class known as saline-chalybeate waters, each spring differing somewhat in properties from its fellow. The one most used, known as the "Washington" Spring, contains the carbonates of lime, iron, and magnesia, bicarbonate of sodium and potassium, and chloride of sodium, with traces of iodine and bromide. Free sulphurous acid is present in considerable quantities, and the water is quite heavily charged with carbonic acid gas. The temperature of all the springs, with one exception, is about 56° F. In this single exceptional case, in which the temperature ranges about 10° higher, the waters are used for bathing purposes in rheumatism, with good results. A peculiarity of the Washington or main spring is its eccentric behavior, which seldom fails about the time of the autumnal equinox. It is said that the waters always become turbid at these periods and the same disturbances have been observed after great storms or earthquakes, even though these events occur in regions remote from the springs. The waters are said to remain red with an excess of iron for a short time after these disturbances and then to become harsh and acrid from an excess of alkaline ingredients. The country surrounding Mount Vernon is about equally divided between prairie and timber, a considerable portion of the latter being found on elevated ridges. On the north a belt of timber, about ten miles in depth, affords protection against the winds of winter and causes a considerable modification of temperature. The waters of the main springs are very efficacious in the treatment of dyspepsia, torpid liver, biliousness, and other disorders of the chylopoietic organs. *James K. Crook.*

GREENBRIER WHITE SULPHUR SPRINGS.—Greenbrier County, West Virginia.

POST-OFFICE.—White Sulphur Springs. Hotel and cottages.

ACCESS.—Viâ main line of the Chesapeake and Ohio Railroad direct to Springs. This celebrated summer watering-place is located on the western slope of the Appalachian Mountains, at an elevation above tide-water of more than 2,000 feet. The situation is well within the famous spring region. Within a radius of thirty miles are the Rockbridge Alum, the Hot, the Warm, the Healing, the Sweet, and other well-known springs, while the Natural Bridge, Millboro, the Alleghany, and other resorts are near by. For many years past the Greenbrier White Sulphur Springs have been regarded as a representative summer resort of the South, and it has lost none of its ancient and well-deserved prestige by the development of other springs. As in ante-bellum days, here will still be found the best elements of the social life of the South, with a generous intermingling of Northern beauty and gallantry drawn thither by the numerous attractions of the place. The surrounding scenery typifies the picturesque beauty and grandeur of the Alleghanies. The visitor from the heated and dusty city is at once attracted by the vast lawn of green, velvety turf, shaded by noble forest oaks, luxuriant sugar maples, and venerable pines. Under these monarchs of the forest wild flowers are seen in profusion and in great variety. Among the surrounding mountains are "Kate's" and "Greener," each a mile distant and reaching an altitude of 3,500 feet, and the mountains known as "White Rock," three miles distant, the summits of which form a figure of gigantic size, known as the old "Titan," which, in solitary grandeur, keeps guard like a giant over the White Sulphur. What has been said of other Alleghany resorts applies in full measure to this. The mean annual temperature from April 15th to November 15th is about 63° F., or about the same as the mean annual temperature of Naples, Nice, and the Madeira. The atmosphere is salubrious and invigorating, and at no time excessively warm. The Grand Hotel, with its one hundred cottages, gives accommodation to an immense number of visitors. There are two important springs here, viz., the famous old "White Sulphur," and the "Chalybeate." The Sulphur Spring yields 1,800 gallons of water per hour, and this amount does not vary even during the longest spells of wet or dry weather. It has a uniform temperature of 60° F. An analysis by Prof. A. A. Hayes, of Boston, shows the following mineral contents:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Calcium carbonate	7.07
Magnesium sulphate	35.42
Calcium sulphate	78.35
Silicates	3.46
Magnesium chloride	1.00
Organic matter	4.36
Total	129.66

Gases.	Cubic Inches.
Carbonic acid	11.28
Sulphureted hydrogen	.24
Oxygen	.48
Nitrogen	4.64
Total	16.64

This analysis was made many years ago (1842), and a newer and further analysis is desirable. The water acts on the kidneys, bowels, liver, and skin. As a diuretic its effects are very soon apparent; but some days are

usually required before it produces a decided action on the bowels. Its operation on the liver, too, may not be manifest for some time, and when there is much sluggishness of this organ some auxiliary medication is required. Its effect upon the skin is very apparent, though not immediate. The analysis does not fully explain another important action of the water, an effect which has been attested to by several generations of qualified medical men. This is its alterative power, or that peculiar influence by which it effects a salutary alteration in the blood, in the various secretions, and upon the numerous tissues of the body. No general directions can be given for the internal use of the water. The hours, the quantity, and the period for which the water should be drunk depend upon the individual requirements of the case, and should be ascertained by consulting a physician experienced in the use of such waters. Combined with the influence of the favorable surroundings, the use of the water often proves curative in obstinate cases of chronic bronchitis, in hay fever, in bronchial asthma, and in nasal catarrh. Conjoined with the use of the hot sulphur baths it is of decided value in rheumatism and gout, and is an efficacious adjuvant in the treatment of tertiary syphilis, chronic metallic poisoning, and dartrous skin diseases. According to Dr. Moorman, for many years the resident physician, the water is contra-indicated in organic heart disease, carcinoma of the stomach, and phthisis pulmonalis. The water never proves beneficial when it persistently excites the frequency of the pulse. The water used for bathing flows from the sulphur spring. The bathing establishment has recently been greatly enlarged and remodelled, and it is now believed that it will prove in all respects satisfactory to those wishing to avail themselves of its use.

The Chalybeate Spring. About forty rods from the White Sulphur Spring is a chalybeate spring in which iron exists in the form of carbonates. For the last twenty years this water has been considerably used by a number of visitors who require a ferruginous tonic, and its effects have realized the early hopes that its discovery created. It has not been fully analyzed. *James K. Crook.*

GRINDELIA.—CALIFORNIA GUM-WEED. *Rosin-weed.* "The dried leaves and flowering tops of *Grindelia robusta* Nutt. and of *G. squarrosa* Nutt. (fam. *Compositæ*)" (U. S. P.). These are large and coarse, perennial, resinous herbs, of the far western and southwestern United States. The former was first introduced, then the latter, as possessing different properties. It being quickly determined that the properties were similar, they were united under one title. Nevertheless, many physicians prefer the *G. robusta*. It is much scarcer and more difficult to obtain, and the other is very commonly supplied, broken up or otherwise treated to make a distinction, when robusta is specifically called for. A good mark of distinction is given below. The following is the official description:

Leaves about 5 cm. (2 inches) or less long, varying from broadly spatulate or obovate to lanceolate, sessile or clasping, obtuse, more or less coarsely and sharply serrate, often spinosely toothed or even laciniate-pinnatifid, pale yellowish-green or yellow, very smooth, finely dotted, resinous, thick and brittle; heads many-flowered, the involucres of many series of imbricated scales with acute, spreading or recurved tips. The heads of *G. squarrosa* are mostly longer than broad, contracted-campanulate or conical-urceolate; those of *G. robusta* are broader than long, depressed-urceolate. Ray-florets deep-yellow, ligulate, pistillate; disc-florets yellow, tubular, perfect; pappus of two or three mostly unequal awns, about as long as the disc-florets; odor balsamic, slightly narcotic; taste resinous and gummy, pungently aromatic, somewhat bitter. The quality is roughly indicated by the amount of resinous matter exuded upon the surface.

Resin is the principal constituent. There are also a little volatile oil, wax, gum and tannin, together with a bitter glucoside, in small amount. Its uses are external and systemic. The fluid extract, if painted upon a surface poisoned by rhus and similar agents, is one of our best remedies. It forms a dry coating which excludes the irritating atmosphere and prevents the spread of the poisonous fat, probably also absorbing it into the resinous film. It is of some similar use for treating burns and as an injection for urethritis and vesical catarrh. Its internal action, as a sedative expectorant, is not so readily explained. It is largely used, by way of the stomach, in chronic and subacute bronchitis, in asthma, and in whooping-cough. It is mostly given in the form of the official fluid extract, in doses of 1 to 4 c.c. (fl. ʒ ¼ to i.).

Hysterionica or *Baylahuen*, the herb of *H. Baylahuen* (Gay) Baill. (*Haplopappus B.* Gay) is a Chilian drug, very closely related, botanically, chemically, and physiologically, to grindelia. It contains a large amount of a brown, odorous, somewhat acrid resin and an essential oil. It is considerably used at home as an anti-diarrhœal and anti-dysenteric, and was introduced to Europe and the United States about the year 1890. Repeated trials showed it to possess some value in ameliorating the diarrhœa of phthisis. At the same time, it was found to act as a sedative diuretic and not to produce gastric irritation. The fluid extract was given in ɱ x. doses every six hours, and the administration prolonged. The drug has not come into general use. *Henry H. Rusby.*

GRIPPE, THE.—See *Influenza.*

GROWTH.—This article is divided for convenience into four sections: I. Definition of growth. II. Growth as a function of cells and tissues. III. Human growth statistically considered. IV. The laws of mammalian growth.

I. DEFINITION OF GROWTH.—Definitions of growth are almost as numerous and various as the writers on the subject. Among these we may distinguish two principal points of view. According to one of these, growth is defined as increase of size or volume. From this point of view any increase of volume is growth no matter to what cause it may be due, and differentiation is regarded as an entirely distinct phenomenon which may or may not accompany growth.

From the other point of view the term growth implies in a general way an increase in the number or size, or in both, of the histological elements; and also, but more vaguely, implies that the elements advance, or at least remain stationary in the scale of organization. In other words, if the increase in volume be due to developmental processes, or if it be accompanied by progressive differentiation, it is growth. But if, on the other hand, increase of volume be due to the deposition of products of degeneration, as, for example, fat, it cannot properly be regarded as growth. This definition is not so definite as the first, which, therefore, should be preferred.

II. GROWTH AS A FUNCTION OF CELLS AND TISSUES.—It is evident that the growth of an organism is the sum of the growths of its tissues, and the growth of the tissues depends on that of the cells; hence growth ultimately rests upon, first, the increase in size of single cells, and, second, the multiplication of cells. Owing to their peculiar mode of growth, the plants afford the best material for the study of the process in its simplest form. At the tip of each stem or rootlet there is a mass of cells in an embryonic condition, and during rapid growth these cells undergo frequent cell division. There is at the extreme tip a cell or a group of cells that always divide by a transverse partition into a distal and a proximal daughter cell or cells. The daughter cell at the tip, the distal one, remains in an embryonic condition and divides again in the same manner. In this way the proximal daughter cell becomes separated from the tip by the successive divisions of the apical cell or group of cells. If we follow one of the proximal cells through its life history, we shall see that it at first divides repeatedly, forming a group of small cells with dense protoplasm and thin cell walls. This is the period of most rapid multiplication. A little later the process of cell division becomes less frequent in this group, and the