as a biologic unit; Hoche (1899) had admitted that the histologic unity of the neuron could no longer be upheld, but urged that it was a functional-trophic unit. Münzer (1899) took the stand that the neuron doctrines were better founded than ever, and that the criticisms of Nissl and Bethe were without weight. Auerbach (1899) supported a modified neuron doctrine, while Semi Meyer, von Lenhossék, van Gehuchten, and Ramón y Cajal could see no reason for changing the original conception and doctrines. Max Verworn, in a collective review read before the German Society of Naturalists in 1900 took almost precisely the stand I took in 1899. The two longest publications of the anti-neuronists are those of Bethe (1903) and Nissl (1903). Bethe's book,⁷ while it represents a vigorous attack on the neuron doctrine, embodies the results of most interesting and important original researches, and should be carefully read by every neurologist. Nissl's large volume,⁸ which was reviewed for the *Psychological Bulletin* by Dr. Adolf Meyer, is devoted entirely to controversy and is looked on by ardent neuronists as a sort of attenuated curse of St. Ernulphus on the neuron doctrine and its supporters.

In December, 1903, by good fortune, I happened to be in Madrid just at the time when Ramón y Cajal⁹ announced his discovery of a new and easy method for demonstrating the neurofibrils. He kindly showed me his preparations, which made clear at a glance that a flood of new light was at once to be thrown on these remarkable constituents of the nerve cells and nerve fibers (Figs. 6, 7 and 8). His method is simple, is easily applicable to invertebrate as well as to vertebrate tissues and to the embryonic nervous system as well as to that of the adult. It stains the fibrils much more perfectly than is possible with the methods of Bethe and Apáthy, and has the further advantage that it leaves the glia entirely unstained. A somewhat similar, though more complex, method, devised independently and almost simultaneously by Bielschowsky¹⁰ of Berlin, is also now much used for demonstrating the neurofibrils. The finest fibrils are said to be best shown by still a third method, that of the Italian investigator, Donaggio¹¹ (Fig. 9).

Let us now turn to an examination of the principal points which have been under discussion of late and see what is the actual state of knowledge concerning them.

(a) *The Neurofibrils, Golgi Nets and Interneuronal Relations.*—Studies by the methods of Cajal and Bielschowsky and by the method of Donaggio have shown how rich and delicate the network of neurofibrils in the nerve cells is. Bethe's method stained only the coarser strands, which, therefore, looked like isolated fibrils. The newer methods demonstrate finer fibrils, forming anastomoses among these. Bethe's schemata (Figs. 10,

11, 12 and 13) of varying arrangements of neurofibrils as the animal scale is ascended are not confirmed by these newer methods. On the contrary, the nerve cells as regards the neurofibrils are similarly built throughout the whole animal series. There appear to be no independent neurofibrils, but only neurofibril networks embedded in the nerve-cell protoplasm (see figures). The network extends through the whole neuron, but the mass of the network may increase or diminish in size in various parts. Thus there is a large fibril network in the cell body, and this is connected by the attenuated fibril network of the axon, with expansions of the network in the terminal fibers. The so-called "end-feet" of Held are now known to be identical with the terminal buttons of Auerbach, and these, ending on the surface of the cell body and dendrites, are exquisitely demonstrated by Cajal's method (Fig. 14). I have placed a specimen under the microscope illustrating them. These terminal buttons contain neurofibril networks. Nowhere, in specimens stained by Cajal's method or by Donaggio's method, in the cell body or in the terminal buttons, thus far have the neurofibrils been seen actually at the surface; it is stated that there is always an area of fibril-free protoplasm between the networks and the cell boundary.

These recent methods which stain the neurofibrils so exquisitely do not reveal any extraneuronal neurofibrils whatever, either in the region of Nissl's "nervous gray" (Cajal, Retzius) or in the so-called point substance or neuropile of invertebrates (Cajal, Retzius) (Fig. 15). The whole area of Nissl's nervous gray appears in Cajal's specimens as a feltwork of dendrites and terminals and collaterals of axons containing neurofibrils within their protoplasm. The Golgi nets do not stain at all with Cajal's neurofibril method. Moreover, Held, by other methods, has concluded that they are derivatives of the glia; both he and Donaggio deny their nervous character. There is some evidence that the terminal buttons, to which I have referred, reach the protoplasm of the nerve-cell body by lodging in the meshes of the Golgi net. No one has been able to demonstrate any relation between neurofibrils and Golgi nets. In the light of these newer studies the enormous importance attributed by Bethe and Nissl to the Golgi nets seems, therefore, to have been premature; their views are unsupported by facts.

(To be continued.)

THE BLOOD-CLOT DRESSING IN MASTOIDECTOMY, CONSIDERED PHYSIOLOGICALLY.*

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That the special surgeon can profit largely by keeping in close touch with general surgery is generally admitted, but that all surgeons would gain immeasurably from as intimate an alliance with physiology as they have established with anatomy and pathology is a fact, perhaps, not so well recognized. Commenting on this matter, in his last review of surgery, in the December number of *Progressive Medicine*, Dr. Bloodgood alludes to the fact that the physiologist, not specially interested in practical surgical questions and not brought into contact with the daily vital problems confronting the oper-

7. Bethe, A.: *Allgemeine Anatomie und Physiologie des Nervensystems*. Leipzig, 1903, pp. 1 to 488.

8. Nissl, F.: *Die Neuronen lehre und ihre Anhänger*, Jena, 1903, pp. 1 to 478.

9. Ramón y Cajal, S.: "Un sencillo método de coloración del retículo protoplasmico e sus efectos en los diversos centros nerviosos de vertebrados e invertebrados." *Trab. del Lab. de investig. biol.*, Madrid, 1903, vol. ii, No. 4; also, Translation by Azonlay, *Bibliogr. anat.*, Par. and Nancy, 1905, vol. xiv, pp. 1 to 93.

10. Bielschowsky, M.: "Die Silberimprägnation der Neurofibrillen," *Neurol. Centralbl.*, Leipzig, 1903, vol. xxii, p. 997 to 1006; also "Ein neues Imprägnationsverfahren zur Darstellung der Neurofibrillen," *Arch. f. Psychiat.*, Berlin, 1905, vol. xxxix, pp. 1321 to 1323.

11. For an epitome of Donaggio's method and work, see Donaggio, H.: "The endocellular fibrillary reticulum and its relations with the fibrils of the axis-cylinder," *Rev. Neurol. and Psychiat.*, Edinb., 1905, vol. iii, pp. 81 to 100.

* Read before the Southern Section of the American Laryngological, Rhinological and Otolaryngological Society at the annual meeting, held in Norfolk, Va., 1906.

ating surgeon, during his scientific investigations, learns many physiologic facts which would be of great value to the surgeon, yet, with the rarest exceptions, this valuable information is lost, so far as the practical surgeon is concerned. An occasional collection and fitting together of bits of knowledge gained in the course of many physiologic investigations, studies made perhaps without a thought of their bearing on surgery, might enable us to elucidate some of the important problems with which the surgeon has to deal. The possibilities of such a plan occurred to me some months ago while listening to a discussion on the treatment of mastoiditis and, being deeply interested in the blood-clot dressing of the mastoid wound, I determined then to consider from the physiologist's point of view the advisability of employing that method.

It is only a few years since aural surgeons were discussing with great animation the proper method of procedure for the opening of the mastoid process when diseased. To-day we do not debate over the propriety of a simple incision in the overlying soft tissues, a small perforation in the outer cortical layer of the bone or the more extensive invasion of the mastoidal cellular structure; unanimity of opinion has been reached on that point. The history of the development of the operation of mastoidectomy has been furnished us in a most interesting and entertaining way by Dr. Whiting, and we will certainly all agree with him without cavil, however we may differ in the details of performing the operation, in the dictum that the operation of the present period has for its prime object the complete and immediate eradication of all the diseased tissue. In other words, in every operation for mastoiditis the surgeon now endeavors to remove every particle of pus, detritus and necrotic or carious bone, even though he be compelled to obliterate the cellular structure of the tip, the zygomatic process and the occipital region, or to invade the cranial cavity itself. Assuming that all this has been accomplished, however, does it constitute a complete operation?

I think we may accept as applicable to mastoid surgery a statement made by J. Collins Warren,¹ with reference to osteomyelitis, that: "Modern surgery demands a complete operation; that is, one which insures rapid and permanent healing of the wound." Permanent healing of the wound will usually follow such an operation as is referred to above, but rapid healing is not so commonly assured. The ideal operation might be described as one which gives the greatest promise of a cure in the shortest possible time and at the least expense of comfort to the patient. If a mastoid wound be dressed with sterile or antiseptic packing at the time of operation, the period of healing will vary from three weeks to several months; very rarely will complete closure occur in less than this time, and I have frequently seen cases that required dressing over a period of six months. It can not be denied, either, that these dressings are often distressingly painful to the patient and always time consuming and more or less annoying for the surgeon. If a method of dressing the wound can be devised which will promote rapidity of healing without additional risk to the welfare of the patient, it will certainly add very materially to the comfort and happiness of both patient and operator. Such a method, I believe, has been provided for us in the blood-clot dressing, first recommended for use in the mastoid

operation by Dr. Clarence J. Blake, of Boston, with whose papers on the subject all of you are doubtless familiar.

The primary object of this dressing is to obtain healing of the wound by first intention, but, when this occurs, other advantages accrue; for instance, the normal contour of the mastoid process is restored, the resulting scar is a mere line which is entirely hidden from view by the auricle, and the period of healing is reduced to five or seven days, with practically no after-treatment. No deformity, almost no scar, and primary union constitute, on the whole, a stake worth playing for. On the other hand, in cases in which the blood clot fails to organize, there is no additional risk to the patient; should the wound not have been so clean as was supposed or should the clot become infected in any one of various possible ways, it simply breaks down and the wound has to be opened, cleansed and packed in the usual way, the patient then being in practically the same position he would have occupied had the open method been employed primarily.

With the modern teachings of surgery constantly before us, that all pus cavities should be treated as open wounds and compelled to fill up by granulation from the bottom, it is not surprising that this suggestion of Dr. Blake should have been received with skepticism. As I have talked with my confrères or listened to the discussion of the subject in otologic congresses, it has seemed to me that men hesitated to employ the method, first, because of a fear of the possible consequences of inclosing in the wound some microscopic particles of infective material and, second, because they considered the normal blood clot a favorable medium for the growth of bacteria. So far the answer to these expressed or implied criticisms has been solely in the nature of relating clinical experiences. A certain percentage of excellent results have been shown by those who have used the blood-clot dressing and as yet no one has related any unpleasant experience.

It is my purpose to take up these objections from another point of view, namely, to consider what happens when a clean cavity in bone tissue is filled with healthy blood clot, what power such a clot may have to overcome infective material that may have been inadvertently left in the wound, and whether general surgeons have any analogous experiences with other portions of the bony frame work, to assist us in drawing conclusions regarding the mastoid portion of the temporal bone.

Experimental and clinical studies have shown that if any clean wound be filled with the patient's own blood, and safeguarded from later infection, the blood clot tends to organize and new tissue, similar to that inclosing the clot, soon forms to replace the latter. The blood flowing into the wound cavity rapidly clots and the fibrous framework of this clot constitutes a scaffolding on which the new tissue is built. Fresh granulations spring from the walls of the cavity and grow out into the clot, forming a new fibrous connective tissue, the nature of which is further altered to accord with the character of the surrounding cavity walls; that is, if the wound be made in bone, osteoblasts are sent out from the bony walls or from the periosteum to convert the fibrous substance into osseous tissue. The migratory power of these osteoblasts is limited, and they travel only a short way from their starting point, so that, in the case of a large cavity in bone, the newly-formed bone does not extend far from the cavity wall, and the

1. "Surgical Pathology." J. C. Warren, 1895, p. 214.

center of the new-formed tissue remains fibrous in character. It seems quite probable, however, that in a small cavity, such as we ordinarily make in the mastoid process, the osteoblasts, reaching out from all directions, may extend a sufficient distance to meet in the center and thus to complete the construction of a new bony process. Just how early this osteoblastic activity commences is not known, but such cells have been observed to form within forty-eight hours after the operation, and it is certain that granulation tissue grows more rapidly into a healthy blood clot than into space. It is plain, then, that Nature may be greatly aided in the reconstruction of destroyed tissue by providing an excellent framework on which to build and leaving her only the task of furnishing vascularity and new tissue cells.

But, suppose the wound cavity to be treated is not absolutely clean, that some invisible particle of septic material is present when the blood is introduced, has the blood any bactericidal or antitoxic powers? A long series of observations by the most careful investigators has clearly proved that the normal human blood does possess such properties. Metschnikoff, Nuttall, Fodor, Lubarsch, Vaughan and Novy and a host of others have published most interesting work on this subject. From their several experiences we may safely draw the following conclusions: The normal human blood possesses bactericidal power, varying in degree in its antagonism to different micro-organisms; this property of the blood is greater after it is drawn from the vessels than while circulating intravascularly; the microbe-destroying substance is found in the serum, but is produced by the leucocytes; certain chemical changes in the blood may be induced either to increase or to diminish its bactericidal power, and this property of the blood naturally diminishes after the clot is forty-eight hours old.

Nuttall, following a suggestion of Metschnikoff, was probably the first to demonstrate the bactericidal power of normal blood serum. Working under the direction of Flügge, in 1888, he used defibrinated blood taken from various species of animals and found that this blood destroyed the *Bacillus anthracis*, *Bacillus subtilis* and the *Staphylococcus pyogenes aureus* when brought into contact with them. He also confirmed the finding of Fodor that after awhile the blood loses its germicidal properties and becomes a suitable culture medium in which germs grow abundantly.

The fact having thus been determined that the blood serum removed from the body acts far more rapidly and energetically on microbes than the plasma and lymph within the body, the disparity of action was further shown by Lubarsch,² who attempted to ascertain the exact power of the blood of some animal over a given serum; using the bacillus of anthrax and experimenting on rabbits, he injected known quantities into the circulating blood and found that this animal was quite able to take care of a dose of less than 16,000 germs, but if a larger number were injected fatal infection resulted. If he drew a small quantity of blood from an animal of the same class and size into a test tube and inoculated that with the same micro-organism, many times that number of germs were destroyed; that is, one cubic centimeter only of the rabbit's blood serum would destroy more than 16,000 of these germs when inoculated into the clot outside the body, and he could not, after a few minutes, reproduce them by culture from the clot.

Then a most interesting series of investigations followed to determine what element of the blood possessed this bactericidal quality and how it acted. Vaughan and McClintock have presented the most conclusive report on these points, and they hold that the leucocytes secrete some substance which is poured into the serum, that this substance is a proteid, and that the only proteid likely to be present in blood serum to which such properties could be attributed is nuclein.

The clotted blood possesses greater power than the circulating blood probably because in the formation of the clot the leucocytes break down and discharge their entire complement of this nuclein. Other workers have demonstrated the transient duration of this power in the blood clot, a power which seems to diminish rapidly after forty-eight hours, and the fact that certain chemical changes in the clot may cause a variation of its power. The bactericidal power seems to be present in freshly drawn blood only when it is alkaline in reaction. If its alkalinity be raised above normal the bactericidal power will be somewhat enhanced, but if the blood be below normal alkalinity or if it be rendered acid in reaction such power is diminished or actually destroyed. The nuclein acts only in an alkaline serum. Again, if alcohol be added to the blood, the bactericidal property is destroyed through the precipitation of the albuminoid constituent. Bichlorid of mercury, likewise, has a deleterious influence on the bactericidal property of blood serum.

These chemical experiments have an important bearing on the use of blood clot as a surgical dressing.

The use of carbolic acid and alcohol for the cleansing of the wound, as an extra precaution of cleanliness, prior to the introduction of the blood, has been recommended by some surgeons, but it seems not unreasonable to venture the suggestion that some of the failures with the blood-clot dressing may have been due to excessive zeal in the use of carbolic acid and alcohol for antiseptic purposes. If exact neutralization were possible and the wound left in a neutral state, no harm could result from the employment of these substances, but if there be left any measurable quantity of either it militates against success. On theoretical grounds it would appear more rational to rely on dry cleansing of the wound with instruments and sterile sponges, or to wash the cavity with sterile salt solution which, if it produces any effect on the coming clot, renders it more alkaline and increases its power to control septic material.

Leaving the realm of experimental medicine and turning to practical surgery, we find, again, the strongest possible indorsement for the employment of healthy blood clot in the healing of wounds. Most physicians are familiar with the epoch-making report of Schede, "Ueber die Heilung von Wunden unter dem feuchten Blutscharf," or know of the most excellent results obtained by Halsted and his associates in the treatment of osteomyelitis by this method. The whole subject was excellently presented by Professor Halsted several years ago and, as there is no higher authority, I could do no better than quote from his paper.³

After reviewing the objections to leaving blood in wounds and the bearing of Lister's work on the subject, he says:

"Although perfectly familiar with the organization of the

2. Allbutt's System of Medicine, vol. i. p. 89.

3. Johns Hopkins Hosp. Reports, vol. II, p. 255-261.

blood clot, it apparently never occurred to Lister to make a systematic effort to utilize the blood clot and to imitate Nature's method of disposing of the dead spaces in wounds.

He has taught us what can be done under the cover of antiseptics. One may maltreat the tissues to any extent, mutilate the wound during the operation in every possible way, cut off by ligatures the circulation in large masses of tissue, produce extensive areas of superficial necrosis by irrigation with antiseptic solutions, stuff the wound with gauze and drainage tubes, tear out the stuffing and with it the granulations which have grown into it, restuff, etc., and still the wound may heal without suppuration, without septic inflammation and in a way which is, perhaps, altogether satisfactory to the surgeon.

But now that wound infection is for many surgeons almost a thing of the past, we may ask ourselves if, after all, our wounds are ideal wounds. One naturally hesitates to attempt to give one's notion of an ideal wound. His ideal wound of to-day may not be his ideal wound of next year or even of tomorrow. I conceive an ideal wound to be one which immediately after the operation is reduced to the condition of a non-penetrating subcutaneous wound, and which is as free as this is from the dangers of infection.

Impressed by the work of Küster, Neuber and others, and entertaining with them the same fears of blood in wounds, it was my practice for several years to attempt with the utmost care to obliterate the dead spaces in wounds. The results were gratifying, but the technic was often very tedious. For example, after an amputation of the thigh it would not infrequently take an hour to obliterate all the dead space. The mechanical problems were sometimes quite difficult, and one was perpetually annoyed by the fear that he might strangulate the tissues included in the sutures. After a time I became convinced that it was impossible to obliterate thoroughly all the dead spaces in some wounds, and I observed that wounds in which the dead spaces were not obliterated healed throughout by first intention just as regularly as did the other wounds. I was, therefore, quite prepared to welcome Schede's article on the healing of wounds under the moist blood scab. This contribution by Schede⁴ I believe to be the greatest which has been made to the technic of surgery since the introduction of antiseptic methods by Lister.

The immortal John Hunter was many years in advance of his time when he expressed himself on scabbing and the organization of the blood clot as follows: "In many deep-seated wounds, where all the parts have remained in contact, those underneath will unite much better if the surface be allowed to scab. Some compound fractures (more especially where the external wound is very small) should be allowed to heal in the same way, for by permitting the blood to scab on the wound, either by itself or when soaked in lint, the parts underneath will unite, the blood under the scab will become vascular and the union will be complete even when the parts are not in contact. Many wounds ought to be allowed to scab in which this process is now prevented, and this arises, I believe, from the conceit of surgeons who think themselves possessed of powers superior to Nature, and, therefore, have introduced the practice of making sores of all wounds."

From these and similar experiments and experiences, I think we are fully justified in using the blood-clot dressing to complete the operation of mastoidectomy, and I only wish to add a few words regarding the technic of its employment. You will infer from what I have said that very little can be done to assist the blood clot in its possible conflict with overlooked septic material, but a good service can be rendered by avoiding some things that would tend to hinder the blood in its beneficent work.

In the first place, the nearest possible approach to absolute surgical cleanliness must obtain throughout the operation. This applies not only to the operator and

his assistants, to the sterilization of all instruments and the protection of the operation field by proper sterile sheets or towels, but also the perfect removal, so far as can be determined, of every particle of infective material and of diseased tissue.

Next, it is exceedingly important that the wound be closed in such a way as to prevent the introduction of new infection and to promote primary union. It is my opinion that a good many failures with the blood-clot dressing have been the result of faulty closure of the soft parts. Shreds of tissue that may be infected or that would prevent neat apposition of the margins should be cut off. Chemical sterilization of the wound should not be attempted. If irrigation is considered necessary, sterile normal salt solution may be employed. Finally, for the closing of the wound, the subcutaneous silver wire suture recommended by Halsted may be used.

All physicians are familiar with the experimental work performed some years ago by Professor Welch on the sterilization of the skin. Making use of the most approved methods of cleansing the skin's surface, he could still secure a bacterial growth from the deeper layers of the corium and he determined that this region was the natural habitat of the *Staphylococcus epidermidis albus*, which germ was the active factor in the production of the common stitch abscess. If the sutures be carried through the skin from side to side of the wound, it not only makes the opportunity for a stitch abscess, but opens up a new avenue for infection of the clot. In many instances this will not be sufficient to cause a breaking down of the clot, but if that blood is having a battle with septic particles within the cavity this may be the last straw needed to cause a breakdown.

Furthermore, in the subcutaneous method of suturing wounds, silver wire is the best material to use because it possesses antiseptic properties of its own. Some years ago Bolton, working in Kelly's laboratory, undertook to ascertain the relative value of suture materials, and he found that the best of all was copper wire and next to this came silver; inasmuch as the latter is, for commercial reasons, most available and the antiseptic properties but slightly different, he recommended the general use of silver. It can be easily and surely sterilized by boiling, while catgut is, under the best of circumstances, unreliable and silk is only less so. With a subcutaneous silver wire thread, lacing the wound from side to side, and not penetrating the skin at any point, one has a suture easy of introduction, perfectly sterilizable, strong enough to bear any traction necessary to secure good apposition of the wound lips, and removable without pain at the proper time. A layer of silver foil over the closed wound, before the sterile gauze dressings are applied, will add something to the protection against septic invasion.

It may be too much to say that the complete operation referred to here and described so well to-day by Drs. McKernon and Bryant, with the blood-clot dressing, will constitute the ideal, but I believe it will come to be accepted as the standard operation of mastoidectomy.

Stokes-Adams Disease in Incipient Paresis.—M. E. Rist (Bull. et. Mem. de la Société Méd. des Hôpitaux) reports a case of Stokes-Adams disease complicating the early stages of parietic dementia of syphilitic antecedents. The relation between the bradycardia and the meningo-encephalitis seemed evident, but he remarks that, while lues is known as a cause of either condition, the combination here seems novel.

4. M. Schede: "Ueber die Heilung von Wunden unter den feuchten Blutschorst." Verhandlungen der deuts. Gesellschaft für Chirurgie, 1886.