

soda; his verdict is that "it is certain that it exerted no specific effect upon the disease."

In the absence of any known specific, our therapeutic resources are reduced to those measures which are best adapted to the control of the most distressing symptoms, and to that watchful care and anticipation of complications which enables us so often to tide a patient safely through the critical stages of an infectious disease, and to save many lives, notwithstanding our acknowledged inability to cure these diseases. Although the high pyrexia is not so immediately dangerous to life as is the case in certain other continued fevers, it will always be advisable to keep it within bounds, and the tendency to death toward the close of the febrile paroxysm, primary or secondary, should be borne in mind. The evidence on record is in favor of sodium salicylate, rather than quinine, as an antipyretic medicine; it may be given to the extent of one hundred grains, or more, in the twenty-four hours, and is said to be well borne. Its persistent use, however, interferes with the patient's appetite, and it will be best to reserve it for those cases which are marked by a specially high pyrexia, and to administer it, in full doses, only when the temperature approaches 106° F. For a more moderate elevation of temperature, cold sponging of the surface, and the administration of simple febrifuge remedies, such as effervescing draught, or solution of spirit of nitrous ether, will suffice. Aconite, in small and repeated doses, may be given—one drop every two hours—in combination with moderate doses of spirit of nitrous ether, and if any routine treatment for the fever is considered necessary this may be recommended, as less liable to disturb the stomach than certain other drugs which are sometimes used in similar conditions, *e.g.*, veratrum viride, digitalis. There is a tendency to constipation, and a mild aperient will commonly be required at the outset of the attack; a dose of castor oil, or a simple saline purgative, will answer the purpose; later the bowels may be moved, if necessary, by enemata; emetics, as a rule, do more harm than good. *Headache* is to be combated by cold applications to the head. *Insomnia* is a marked and distressing feature of the disease; Carter prefers to administer chloral and bromide of potassium for the relief of this symptom, rather than to give opiates. Pepper, on the contrary, says that "opium and morphine must be regarded as the basis of the rational treatment of relapsing fever. It is called for by the insomnia, the severe headache, and the pains in various parts of the body, the nausea and vomiting, and the pyrexia." One-fourth of a grain of morphine, given at intervals of six to twelve hours, was found by the author last mentioned to relieve pain and vomiting, and often to induce refreshing sleep. It is contraindicated in those cases having a typhoid tendency, as shown by a disposition to stupor and deficient urinary secretion. In the experience of Pepper during the Philadelphia epidemic, bromide of potassium in full doses failed to produce sleep or relieve headache, and chloral, in doses of twenty to forty grains, could not be depended upon, although it sometimes gave relief. In view of the tendency to heart failure in this disease, the author named very properly points out the possible danger which may attend the administration of chloral. For the relief of excessive *tenderness of the liver or spleen*, Carter recommends hot fomentations and poultices in preference to cold applications, "which are seldom grateful to the patient." To control excessive *irritability of the stomach*, Pepper advises the use of small doses of calomel, gr. $\frac{1}{4}$ — $\frac{1}{2}$ every two hours, or gr. $\frac{1}{2}$ of nitrate of silver, dissolved in thin mucilage of acacia, administered at intervals of three or four hours. *Hiccough* is a distressing symptom, which often defies all remedial measures. In Pepper's experience, chloroform is the most useful remedy for its relief. As death from *heart failure* may occur at the acme of the pyrexia, or during the depression, often amounting to collapse, which follows crisis, it will be necessary to watch carefully for the slightest indications of such failure, and to guard against it by the administration of digitalis, or strychnia, and the early use of alcoholic

stimulants. When the symptoms of *collapse* are developed, it will be necessary to resort to the subcutaneous injection of ether, or of strychnia, and to apply artificial heat to the surface of the body.

In this as in other specific febrile diseases running a protracted course, it is necessary to commence with a *supporting treatment* at an early date. As soon as the stomach will retain it, liquid nourishment should be administered at stated intervals—every two or three hours: meat broths, milk, or gruel may be given if the condition of the stomach admits of their being retained; if not, koumiss, chicken water, or skimmed milk diluted with lime water, may be given in small quantities and at shorter intervals. When the stomach is very irritable, it is probable that iced champagne, or a teaspoonful of good brandy poured upon broken ice in a glass, and taken as cold as ice will make it, will be found the best form of stimulant. Whiskey toddy or milk punch may be given during the apyretic interval, or until convalescence is fairly established, or a good wine may be substituted for these if the patient prefers. In this disease, as in yellow fever, sudden death is liable to occur from cardiac syncope, as a result of very trifling exertion made when the patient is apparently out of danger. It therefore becomes necessary to insist upon absolute quiet and the maintenance of a recumbent position until such time as the strength of the patient is fairly restored. This precaution is especially imperative at the time of crisis, and during the period immediately following it, when there are a subnormal temperature and other evidence of a state of collapse. *George M. Sternberg.*

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REMITTENT MALARIAL FEVER. See *Malarial Diseases*.

RENNIN.—This name for the milk-curdling enzyme of the gastric juice was first proposed in Foster's "Text-book of Physiology," and is now in common use in English-speaking countries. The name of *chymosin* was that given to it by Deschamps; it was later termed *lab* by Hammarsten, and this name is occasionally used by English writers.

The most valuable researches into its mode of action and isolation are due to Hammarsten, who was the first to show that it is distinct from pepsin. This view is now almost universally accepted, although it has recently been stated by Pawlow that rennin and pepsin are identical. Pawlow's experiments, which consist chiefly in a demonstration of a parallelism of intensity of action of gastric juice in digesting proteid and coagulating milk, are not, however, very convincing against the careful experimentation of Hammarsten in the separation of the two enzymes, as described later on in this article.

Rennin and milk-coagulating ferments allied to it are very widely distributed, for rennin occurs not only in the mucous membrane of the stomachs of all mammalia which have been tested for it, but is also found in the stomachs of birds and fishes where its function is at present unknown. A similar if not identical ferment is found in the cell sap of many plants, such as the butterwort, fig-tree, and artichoke, and in certain of the Schizomycetes.

It is usually prepared commercially as rennet in the form of solution, powder, or tabloids, preserved with boracic acid, from the fourth stomach of the calf; carefully prepared products preserve their power of coagulating milk almost indefinitely, and long after proteid decomposition may have taken place in the other constituents admixed with the rennin.

Rennin is present in man at birth, and in this respect differs from pepsin. In its distribution in the gastric mucous membrane it closely resembles pepsin, being present only in small quantities at the pyloric region. Like pepsin, also, it is present in the gland cells as a zymogen; in fact, it was in the case of rennin that a precursory form or zymogen (Labzymogen) was first demonstrated by Hammarsten in 1872, some years before a similar demonstration was made in the case of pepsin by Langley and Edkins.

The zymogen appears to exist in a more stable form in some animals than in others, for while a neutral extract of the mucous membrane of the sheep or calf contains the enzyme in an active form, similar extracts from birds, fishes, and certain mammalia exert an action upon milk only after these extracts have first been treated with very dilute acid and again neutralized.

Rennin and pepsin and their corresponding zymogens behave very similarly on treatment with dilute alkalies; thus both rennin and pepsin are very rapidly destroyed by traces of caustic alkalies. The active ferments are also destroyed in both cases much more rapidly than their zymogens by the alkaline carbonates in dilute solutions, and this fact has been utilized, especially in the case of pepsin and pepsinogen, for proving the existence of the zymogen.

Rennin differs from pepsin in that it will act in a neutral or even in a faintly alkaline medium, but it acts most quickly when the medium possesses a slightly acid reaction. Excess of acid destroys its activity.

The optimum temperature lies at 37° C. to 40° C.; at this temperature the reaction takes place with three times as great rapidity as at 25° C.; activity ceases at 50° C., but the enzyme is not destroyed very rapidly at this temperature, and becomes active again as the temperature is lowered toward the optimum. The enzyme is destroyed, however, in five minutes when heated to 70° C. in neutral solution, or at 65° C. in acid solution. Its activity is also removed by standing under alcohol, but less rapidly than is the case with pepsin.

That the action is a truly enzymic one is shown not only by the above-mentioned destructions of activity, but also by the fact that it can occur in the presence of antiseptics, and by the infinitesimally small amount necessary to evoke the coagulation, one part of "purified" rennin being capable of coagulating, according to Söldner, ten million parts of casein.

The most successful attempt at its isolation was made by Hammarsten, who utilized Brücke's principle of mechanical precipitation by first neutralizing a gastric infusion with magnesium carbonate which precipitates the greater part of the pepsin. The filtrate was then partially precipitated by solution of acetate of lead to remove the remainder of the pepsin, and finally the rennin was thrown out by further addition of lead acetate and ammonia. This last precipitate was dissolved in very dilute sulphuric acid, and the rennin again mechanically thrown out with stearic acid by the addition of a solution of an alkaline stearate. The rennin was then finally obtained in solution in water by suspending the stearic acid in water and shaking up with ether, which dissolved the stearic acid and left the rennin behind in the aqueous layer.

The solution obtained finally did not act at all upon fibrin, but powerfully coagulated milk in neutral solution. This solution behaved in many important respects differently from a proteid solution, viz., it was not coagulated by heat, did not give a xantho-proteid reaction, and was not precipitated by alcohol, tannin, iodine, or neutral acetate of lead.

The chief facts as to the chemistry of the action of rennin upon milk are to be ascribed also to Hammarsten's researches upon the subject. When milk clots the greater part of the proteid separates in an insoluble form as casein (paracasein of Hammarsten), which entangles all the fat in its meshes as it contracts and so expresses a clear fluid called the whey, while the coagulated casein and entangled fat are called the curd. The whey contains the inorganic salts, lactose, and a small amount of albumen and globulin, which are called lactalbumin and lactoglobulin. Hence the casein is that important constituent which is chemically concerned in the process of coagulation.

The proteid from which the casein is formed in the act of clotting is termed *caseinogen* (casein of Hammarsten), and is present, according to some observers, in suspension in fine globules, and, according to others, as a colloidal solution. This proteid body has the properties of a very weak acid which is in fresh milk present as an alkaline salt; when it is set free from its combination it becomes insoluble. It is naturally so set free in the souring of milk, when lactic acid is formed by bacterial action on the milk sugar, and it is for this reason that sour milk curdles. For experimental purposes, such as the study of the properties of caseinogen and its changes during coagulation, it is best precipitated by the addition of a few drops of acetic acid. It can then be redissolved, after washing away the acetic acid, with distilled water, by the addition of water containing traces of alkali or by rubbing up with precipitated chalk.

As in the formation of fibrin from fibrinogen in blood clotting, it is found that calcium salts are necessary for the coagulation to take place, but more exact research has demonstrated that the rôle of the calcium salt is different in the two cases. For while the calcium salt has been shown by Hammarsten to be necessary for the formation of the *thrombosin* which acts as a ferment in blood coagulation, the same observer has also demonstrated that the calcium salt in milk coagulation does not share in forming the ferment, but has its purpose in a second stage of the reaction in actually combining with the caseinogen which has been modified in the first part of the reaction (soluble casein) to form the insoluble casein.

Hammarsten's two stages can easily be demonstrated by taking either a solution of caseinogen, or pure milk to which a few drops of ammonium oxalate have been added to throw down the soluble calcium salts, adding in either case a few drops of rennet, and then warming in a water bath to body temperature for ten to fifteen minutes, when no apparent change will be observed. Still a change has occurred, for if the milk be now boiled so as to throw the ferment out of action in the subsequent operation, and then a few drops of calcium chloride be added so that there is a calcium salt in solution in the fluid, on warming again for a few minutes a clot forms. Here no ferment action can take place in the second process, and as the addition of calcium salt only, and subsequent warming, produce no effect upon milk which has not been treated with rennin as in the first part of the process, it follows that the rennin must in the first portion of the experiment have formed some soluble modification of the caseinogen, which is then thrown out as insoluble casein in the second portion of the experiment.

Working with caseinogen solutions Hammarsten further demonstrated that in the action of rennin upon caseinogen there is detached from the caseinogen a soluble portion, which he termed "whey-proteid," that does not undergo any coagulation, and hence is found afterward in the clear fluid, or admixed in the whey with the lactalbumin when milk is used instead of caseinogen

solution. This proteid has been referred to as lacto-protein by other workers upon the subject.

The process may hence be summarized as follows: 1. The rennin acts upon the caseinogen of the milk and forms two soluble proteids (calcium salts being absent), "soluble casein" and lacto-protein. 2. The "soluble casein" combines with calcium, when calcium salts are present, so forming casein. 3. In the coagulation of whole milk the casein entangles the fat globules forming the curd, and on contracting presses out the water, inorganic salts, lactose, lactalbumin, lacto-protein, and lacto-globulin which form together the whey.

Benjamin Moore.

REPARATIVE SURGERY.—Plastic reparative surgery is that department of the operative art which contemplates the repair of defects and deformities, congenital or acquired. Limited in its early history to the restoration of parts destroyed by trauma, plastic surgery has, in the course of centuries, widened its range of utility until its present achievements have been carried to all parts of the body covered by the general integument and to many of the cavities lined with mucous membrane. When the nose is destroyed by lupus, the eyelid shrivelled out of all semblance by chronic inflammation, the palate cleft, the fingers webbed, or the arm bound down by the scars of a burn; when a gastric or vesico-vaginal fistula, an eversion of the bladder, or a ruptured perineum makes life a burden—a plastic operation is the only measure of relief.

HISTORY.—The history of plastic operations presents fluctuations of use and oblivion unknown to the generality of operative measures. For its earliest development we must look to the shores of the Ganges, where from time immemorial mutilations of the face were inflicted in the way of punishment or revenge.

Later, the practice became the portion of the potters and brickmakers, who knew nothing of sutures, but retained the parts in position by the application of clay. There is no evidence that the skill of any of the operators of antiquity went beyond the restoration of mutilated noses, or that they attempted the repair of other parts. It is generally believed that before the Christian era the Brahmans had achieved great proficiency in the restoration of noses, forming them from integument brought down from the forehead or transplanted from another individual, and preferably from the gluteal region. What is truth and what is fiction as regards the rhinoplastic skill of the early priests of India, only appears from the recent translations of relevant parts of the *Susruta's Ayurveda*, according to which the nose was formed from the integument covering the cheeks. "The physician takes a leaf the size of the nose to be formed, and, placing it on the cheek for a measure, raises a flap of skin in such a manner as to leave it attached at one part. After vivifying the scarred part the new nose is quickly brought in position, elevated, and retained by placing two tubes in the nostrils."¹ The classical writers of Greece and Rome were for the most part unacquainted with transplantation of skin as a method of relieving defects, which were treated only by freshening the edges by incisions and drawing contiguous portions of skin together.

On the other hand, Celsus certainly entertained a rational idea of the gliding of flaps. He advised that the defect be removed in the form of a square and that two parallel incisions be continued transversely outward and inward, so that the loosened edges might be easily united. If this could not be done, he recommended that two semilunar lateral incisions, which should involve only the skin, be made with the concavity looking toward the defect.²

Although Galen and Paul of Ægina repeated the precepts of Celsus, the little that was known of plastic operations lapsed into an oblivion even greater than that which befell general surgery, and from which it was not recovered for over a thousand years. In 1442 Pietro Lonzano, bishop of Lu, published a statement in the *Annales du Monde* that a Sicilian named Branca had found a new method of supplying the loss of a nose.

Whence he derived his knowledge does not appear. Among the pupils of Branca was his son Antonio, who had improved and extended his father's method by taking the integument from the arm, and by replacing the loss of lips and of ears in the same way. Plastic surgery doubtless spread rapidly in Italy from the time of the elder Branca, since Vesalius, Fallopius, and others make mention of it. It remained, however, for Gaspardus Taliacotius or Tagliacozzi, professor of anatomy at Bologna, to develop plastic surgery to a degree unknown before him, and to publish the first scientific work on it two years before his death in 1599. In it are described his methods of operating and of retaining the parts in position; and the illustrations accompanying the text have been utilized from century to century by almost all authorities who have written upon the subject. A father of conservative surgery in its best sense, respected by his confrères and beloved by his students, Tagliacozzi well merited the marble statue erected after his death in the amphitheatre of Bologna. In this monument he contemplates a nose which he holds in his hand. The methods of Tagliacozzi failed to obtain a permanent foothold—Paré, Fabricius, Heister, and many others denied the possibility of success. A little over a hundred years after Tagliacozzi's death, the art which he had perfected had again fallen into disuse. Dionys, Desault, Richter, and Chopart only mentioned his practices to condemn them. Such was the state of plastic surgery when, in 1794, a Madras journal brought to England the account of a successful rhinoplasty practised by one of the Koomas, who transplanted skin from the forehead. Although the first rhinoplasty in England was made by Lucas, it was not a success. In 1814 Carpué was more successful in replacing the lower portion of the nose. In 1816 von Graefe introduced plastic operations on the Continent, giving preference to the method of Tagliacozzi. Since the last-mentioned date the utility and feasibility of plastic surgery have not been seriously questioned, and particularly within the last twenty-five years so many additions and improvements have been made that the achievements of the present day doubtless eclipse the best efforts of all former masters in this special art. Associated with the more recent progress of plastic operations are the names of Skey, Liston, and Fergusson in England; Sédillot and Jobert in France; Dieffenbach, B. von Langenbeck, Fritze, and Thiersch in Germany; and the elder Pancoast and Gurdon Buck in this country.

INDICATIONS.—Congenital or acquired defects and deformities demand the resources of plastic surgery when, from their exposed position, aesthetic reasons make their removal desirable, or when disturbances of function and impaired utility are plainly due to them in parts that are hidden from view. Hence it is evident that, regarding the imperativeness of plastic operations, cases in which they are indicated may properly be divided into two groups, in which the necessity to interfere varies as much as the end to be obtained. In the first class of cases the operation is designed merely to improve the appearance of the patient by removing a distorting scar, by suturing the fissured lobule of an ear, or by elevating a depressed nose. Here the indications for an operation are far from imperative, and it is not infrequently the impotency of the patient that impels the surgeon to operate. It is well to remember that operations done solely for cosmetic effects are ordinarily the least satisfactory; it is within the experience of almost every surgeon that results obtained by plastic operations in this group of cases, although eminently gratifying to himself and deemed excellent by his colleagues, are sources of deep disappointment to the patients themselves. In the second group of cases the chief indication for operative measures is the repair of defective function or the protection of parts that are exposed. When the absence of the lower lip, destroyed by lupus or noma, permits of the continuous loss of saliva, derangements of the digestion and of the general health necessarily follow. When the lower eyelid is everted or lost, the defect causes characteristic

changes in the eye and face which often make vision imperfect, and the overflow of tears adds the suffering from an eczema to the other ills of the patient. A large urethral fistula at the peno-scrotal angle, while neither disfiguring nor detrimental to health, is a bar to the full exercise of the procreative function. In each of these cases the indication for recourse to plastic surgery is apparent, and its imperativeness is commensurate with the impairment of function caused by the deformity. To this group of cases belong extensive destruction of the lips, the nose, or the eyelids; cleft palate, cicatrix from burns, or webbing of the fingers; fistulae, urethral, vesico-vaginal, or recto-vaginal; lacerated perineum, and exstrophy of the bladder. In this group of cases must also be included those in which the operative production of a defect is to be immediately followed by its closure by plastic means. Thus an ulcer of the leg that has proven refractory to all other means frequently yields to excision and immediate transplantation of skin; or an extensive epithelioma of the lip can be relieved only by extensive ablation of the part, the large defect being at once closed by dermatoplasty.

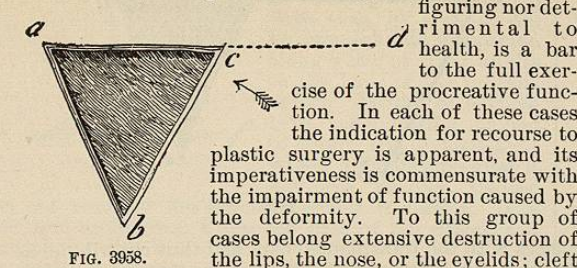


FIG. 3958.

In considering the urgency of a plastic operation, it is necessary to consider the pathological nature of the defect which it is intended to overcome. A loss of substance may be congenital, traumatic, or the result of destructive neoplasms, like lupus, ulcerative syphilides, or epithelioma. In congenital deformities plastic operations are generally not urgently demanded, unless, as in the case of deficiency of the rectum, the life of the child depends upon their correction. But there are milder cases, congenital in character, in which greater deformity can be avoided by early interference. This is true in cases of harelip associated with cleft palate. In simple fissure of the lip the surgeon may abide his time. In complicated cases, on the other hand, early closure of the labial cleft must be advocated, since it has an undoubted influence in approximating the edges of the bony cleft and greatly increases the probability of success in subsequent attempts to close it. In two complicated cases in which I have thus operated during the first week the result was eminently satisfactory. Due regard should necessarily be paid to the general nutrition of the child before a plastic operation of considerable severity and entailing the loss of no slight amount of blood is performed. Defects that are traumatic in origin almost invariably demand removal by plastic operation while the wound is in condition to promise immediate union. This applies particularly to wounds of the face, the soft parts of which are so mobile that they may be stretched to almost any extent, provided the soft structures be thoroughly lifted from the bone. When suppurative processes have been established it is, as a rule, best to delay operative procedures until complete cicatrization shall have taken place. When the loss of substance is inflicted by the surgeon in the removal of malignant growths, its immediate repair is indicated, since there is every reason for believing that when this is accomplished the danger of recurrence of the primary disease is materially decreased. In such cases the all-important object of the operation is the removal of all diseased tissue, irrespective of the size and form of the wound that remains. In the category of defects that result from destructive inflammations, or from tuberculous or syphilitic ulcerations, operative measures are never indicated until the complete cessation of the original disease has taken place. It is in these cases that patients are most importunate in their demands for relief, and injudicious haste on the part of the surgeon is most frequently followed by disaster. Until a lupous or syphilitic ulceration is entirely under control, until, indeed, the whiteness of the cicatrix and

the absence of other evidences of constitutional vice give us reasonable assurance that there is no tendency to recurrence, a plastic operation should not be attempted. An operation too soon performed will often give a new impetus to a disease that has simply been dormant.

NOMENCLATURE.—A number of terms have been suggested as suitable for designating plastic operations. French and German writers generally prefer the word autoplasty (*αὐτός*, self, and *πλάσσειν*, to form). In rare cases, in which the transplanted tissue is taken from a subject other than the patient, this term is evidently inappropriate. To overcome this objection, Velpeau and Guérin have suggested the word anaplasty, signifying to form anew or again. In this country and in England these terms have been generally discarded for the less objectionable one of plastic surgery. When, however, such an operation is performed for the repair or new formation of a particular part, the latter properly gives to the operation a particular name. Thus the formation of a nose is called rhinoplasty; of the lip, cheiloplasty; of the eyelid, blepharoplasty; of the mouth, stomatoplasty; of the urethra, urethroplasty, etc. The scope of this article will not permit the consideration of all the plastic operations. Those of the palate, fingers, urethra, perineum, and vagina are treated of in other parts of the HANDBOOK, while in the following pages will be studied the principles underlying plastic operations in general, and the methods of repairing deformities and defects of the face only.

The underlying basis of plastic surgery is the inherent vitality of the various tissues of the body. This permits them, after partial or total separation, to maintain an independent existence for a greater or less period, and to form new and permanent attachments when brought into contact with freshly wounded surfaces in proximity to, or at a distance from, their original sites. The introduction into defects of strips of epidermis, of the cutis vera, of tendon, of nerve, or of bone, which have been entirely severed from their former connections, constitutes transplantation or grafting. In plastic operations proper, this severance is never complete, a small bridge always being left through which the part to be utilized in the closure of a defect continues to live under the influence of the circulatory, and probably, also, of the nervous, apparatus of the structures whence it was taken, until perfect agglutination in its new position ensues. This occurs in from twenty-four to forty-eight hours, when no untoward complications in the process of wound repair supervene. By the end of a week the union is solidified by the free interchange of blood-vessels between the edges of the defect and the part inserted into it. In wounds of skin more than in those of any other structure there is a manifest tendency to early and firm repair, without which plastic operations would rarely succeed.

METHODS.—The pathology, nature, and extent of a cutaneous defect, and the condition of contiguous parts, will direct the surgeon in the choice of one of a number

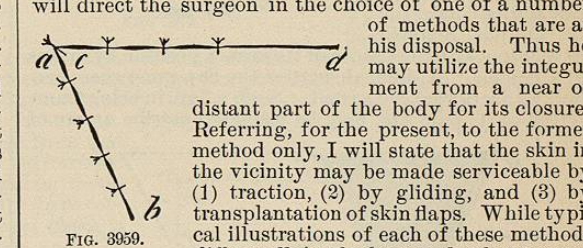


FIG. 3959.

of methods that are at his disposal. Thus he may utilize the integument from a near or distant part of the body for its closure. Referring, for the present, to the former method only, I will state that the skin in the vicinity may be made serviceable by (1) traction, (2) by gliding, and (3) by transplantation of skin flaps. While typical illustrations of each of these methods differ sufficiently from each other to warrant a separate consideration of each, it is well to bear in mind that in their practical application the simpler often verges into the more complicated procedure.

1. The method of closing a cutaneous defect by traction on the vivified edges of the integument surrounding it is based on the extent to which skin can be stretched and yet retain its vitality. This is well illustrated after removal of the breast, in which even the largest wounds can ordinarily be readily closed. In the surgery of the