the pectoral muscle. The long thoracic artery generally runs along the lower border of the lesser pectoral.

In rare cases the great pectoral muscle is wanting altogether, or the clavicular portion alone may be wanting. The lesser pectoral may be attached to as many as five

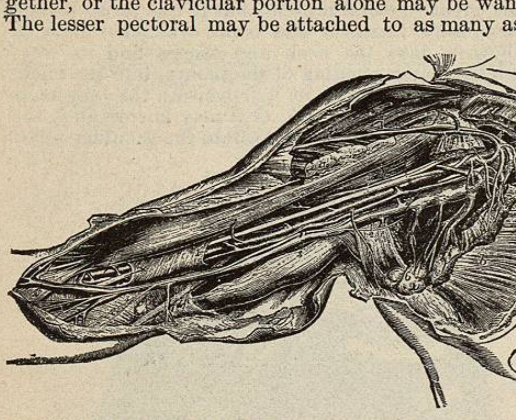

FIG. 4296.—Dissection of Axilla, showing the Axillary Vein (2, 2) and Parts in Relation with it. 1, 1, Axillary artery; 2, 2, axillary vein; 3, 3, basilic vein; 4, cephalic vein; 5, 5, pectoralis minor; 6, axillary glands.

ribs or as few as one. Its insertion may be transferred from the coracoid process to the coracobrachialis muscle or humerus itself.

The *posterior boundary* of the axilla is formed by three muscles which are supplied by the same set of nerves, viz., the three subscapular, and all three muscles are internal rotators of the humerus. The tendon of the latissimus dorsi, with the teres major, forms the lower edge of the posterior fold, the posterior wall of the deeper portion being principally formed by the subscapularis. The axillary vessels rest on this posterior wall, held together by a dense cellular sheath, and separated from the rest of the axilla by the above-described suspensory fascia.

The *internal boundary* of the axilla is formed by the ribs, intercostal muscles, and the upper digitations of the serratus magnus. On this wall, which is somewhat convex, a large nerve is seen running down in a vertical direction, to be distributed to the serratus magnus muscle. This nerve is a branch of the brachial plexus, and is called the long thoracic. We also find here branches of the posterior and long thoracic vessels. Abscesses and tumors, as a rule, lie along this wall, and are fortunately well away from the axillary vessels; in removing tumors we always dissect toward the inner wall.

The *external boundary* of the axilla is formed by the upper part of the humerus and coracobrachialis muscle; along this boundary, and on the inner side of the coracobrachialis are seen the axillary vessels and nerves closely bound down by their fascial covering.

The *inferior boundary* or *base* of the axilla, which is formed by the skin and fascia stretching between the anterior and posterior folds, has already been described.

The apex of this cone-shaped space may be said to be continuous with the posterior triangle of the neck, as vessels, nerves, lymphatics, cellular tissue, and fascia reach the axilla from the neck through this apex. It is the space between the upper edge of the scapula, clavicle, and first rib. Abscesses of the neck have been seen passing through this opening and pointing in the axilla.

Contents of the Axilla.—The axillary vessels, with the lymphatic glands, fat, and loose cellular tissue, are the principal contents of the axilla. The loose cellular tissue permits of free movements of the arm to and from the body, but it also permits of the collection of large quantities of blood and pus. The vessels and nerves are bound together by a sheath of thick cellular tissue; they lie on the outer wall of the space internal to the coracobrachialis.

Axillary Vein (Fig. 4296).—This is the most superficial of the contents of the axilla. In the upper part of its course it is so fixed by fascia connecting it with the coracoid process and pectoralis minor muscle, that if wounded it tends to gape, and air is apt to enter. The vein is formed by the junction of the venæ comites with the basilic vein. This union may occur low down or high up; the normal point of union is at the lower edge of the subscapularis muscle, though the junction not infrequently takes place higher up, sometimes as high as the clavicle. It is always shorter than the artery, measuring about 7.5 cm. (3 in.) in length. Union occurring high up complicates operations upon the artery, owing to the numerous transverse comumnicating branches which cross the artery. The vein lies to the inner side of the artery, and generally overlaps it. When the arm is drawn away from the side it almost altogether covers the artery. In the course through the axilla, this vein receives many tributary branches, the largest of which is the subscapular. It receives the cephalic vein immediately above the lesser pectoral muscle. In operations on the axilla, the vein and its branches are frequently wounded—more often than the artery—but it is rarely injured by external violence. In reducing dislocations of the shoulder, and using extreme traction, the artery is much more frequently injured than the vein, owing to its proximity to the heart and its fixed position; the vein, when wounded, bleeds freely, and there is great danger of air entering it. This accident has many times occurred, especially in operations for removing diseased glands, and not a few fatal cases are on record. It is always well before dividing the veins, especially about the neck and axilla, to tie them with a double ligature and cut between.

In almost all diseases of the axilla there is swelling of the arm caused by pressure on the veins and absorbents.

Axillary Artery (Fig. 4295).—This vessel, which is the continuation of the subclavian, extends from the lower border of the first rib to the lower border of the teres major muscle; it measures about 15 cm. (6 in.) in length, and its direction is altered with the position of the arm. When the arm is close to the side, it forms a curve having its convexity upward and outward; when the arm is held at right angles to the body, the artery is in almost a straight line; and again, when the arm is held above the head, the slight curve thus formed has its concavity upward. Its upper portion lies close to the chest and rests on the upper serrations of the serratus magnus; the long thoracic nerve is behind it, and in front is the costo-coracoid membrane. Its lower part lies principally on the subscapular muscle. The vein is super-

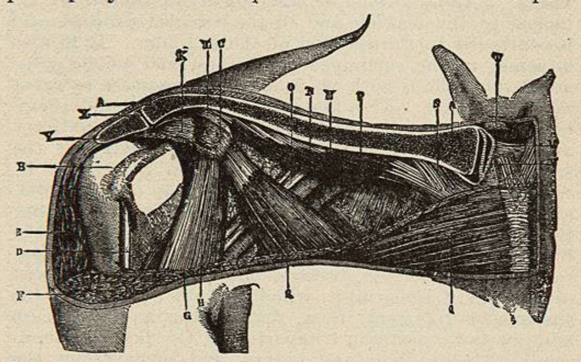

FIG. 4297.—Portion of Clavicle and Acromion Process removed with Pectoralis Major and Deltoid Muscles. Pectoralis minor muscle (*R*) crossing the space; relation of axilla to the shoulder shown, and also contents of axilla; *M*, axillary vein; *N*, axillary artery; *O*, brachial plexus; *P*, subclavius muscle. (From Anger's "Anatomie Chirurgicale.")

ficial to the artery above, and the nerves of the brachial plexus lie to its upper and outer side; lower down the vein becomes more internal and the nerves surround the vessel, the two heads of the median embracing it. For convenience of description the ayillary artery is divided surgically into three portions—the part above,

that beneath, and that below the pectoralis minor muscle. It lies deepest above this muscle and is most superficial below it. The large thoracico-acromial branch is given off immediately above the pectoralis minor, and might be wounded in the operation of tying the axillary in its first part. A number of small branches are given off which are not surgically important. The subscapular artery, given off near the lower edge of the subscapular muscle, is a large branch, which runs to the side of the chest and near its origin gives off the dorsalis scapulæ. The external mammary is given off below the lesser pectoral, and is sometimes of large size; it is always cut in the operation of excision of the breast, and may give rise to slight hemorrhage. The circumflex arteries closely embrace the neck of the humerus, and should be looked for and avoided in excision of the head of the humerus. In wounds of the first part of the axillary artery the vein is so closely in relation with it that it rarely escapes; lower down the artery may be wounded and the vein remain intact. Wounds of the axillary artery may result from stabs, fracture of the neck of the humerus (Fenwick), violence during the reduction of old dislocations. Hemorrhages may be slight or severe, according to the size of the wound. The loose tissues of the axilla admit of great and rapid distention by bleeding from either vein or artery. The treatment is first to compress or temporarily ligature the third part of the subclavian and then cut down on the artery in the axilla, turn out the clots, and ligature above and below the wound in the vessels. It is well to remember that in reduction of an old dislocation the artery has been torn when simple manipulation was practised, owing to the adhesions which had formed between the capsule and the vessel. The artery is usually tied in the third part of its course, where it is most superficial. It has been tied on the first part, but owing to its depth and the thick covering of muscle, and also its close connection with the vein, ligature of the third part of the subclavian is preferred, as being the safer and simpler operation. The third part of the subclavian is more easily compressed than the first part of the axillary.

Aneurism not infrequently affects the axillary artery; this is, perhaps, owing to its nearness to the heart and to the curve the artery makes at its upper part. It has been occasionally ruptured in reducing dislocation of the shoulder.

Nerves of the Brachial Plexus (Fig. 4295).—These nerves are derived from the lower four cervical and first dorsal. They are to the outer side of the artery in the first part of its course, but lower down they surround it. When the axillary artery divides into two trunks, one of which gives off all the branches, this latter is, as a rule, embraced by the two heads of the median. The axillary nerves are rarely torn by traction on the limb; when forcibly stretched they may be torn away from their attachment to the cord in the cervical region, as in a case recorded by Flaubert, where this accident happened in endeavoring to reduce a dislocated shoulder. The median is the nerve most frequently injured in wounds of the axilla, the musculospiral, from its very deep and protected position, always escaping. The axillary nerves are occasionally injured in fracture of the neck of the humerus, and may be compressed in dislocation of the shoulder.

Lymphatics (Fig. 4298).—The axilla is richly supplied with lymphatic vessels and glands. The glands, which are ten or twelve in number, are mostly placed along the axillary vessels and form a continuous chain with the cervical glands. They receive the lymphatics of the arm, and are often much enlarged in inflammatory affections of the hand and arm. A few glands are situated on the serratus magnus muscle and near the lower edge of the pectoral muscles. When enlarged these glands may be felt under the axillary border of the pectoralis major. The lymphatics from the pectoral group of glands drain into the axillary glands as do the lymphatics from the subscapular group. They receive most of the lymphatics from the side of the chest and mamma, and also the superficial lymphatics of the abdomen as low down as the umbilicus (Treves). These are the glands which are first enlarged in certain affections of the breast, *e.g.*, cancer, and also when the chest or abdomen is inflamed superficially, as from blistering, etc. Their efferent vessels join the axillary glands. There are some glands situated at the back of the axilla along the subscapular vessels; these receive the lymphatics from the back. In the interspace between the great pectoral and deltoid muscles near the clavicle, one or two small glands are found; they receive the lymphatics of the shoulder and outer side of the arm; above, they are connected with the lower cervical, and below with the axillary glands. The efferent vessels of the axillary glands pass up with the subclavian vein and join the thoracic duct on the left side, and on the right the lymphatic duct of that side. Sometimes they open separately into the subclavian vein. The

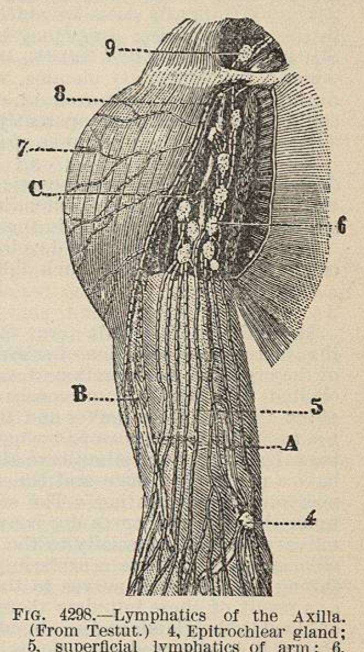

FIG. 4298.—Lymphatics of the Axilla. (From Testut.) 4, Epitrochlear gland; 5, superficial lymphatics of arm; 6, axillary glands; 7, lymphatic of shoulder; 8, lymphatic trunk accompanying the cephalic vein; 9, glands of neck; *A*, basilic vein; *B*, cephalic vein; *C*, axillary vein.

axillary lymphatics which pass upward under the clavicle anastomose freely with the subclavian lymphatics and the lymphatics of the deep cervical glands.

The glands of the axilla are frequently enlarged from sympathy with disease or inflammation of neighboring parts, and not infrequently run on to suppuration. They may be the subject of cancerous infiltration when the breast is affected with malignant disease; occasionally, malignant disease first affects these glands. Scrofulous enlargement of the axillary glands is not uncommon, and their removal is sometimes called for. Professor Verneuil (*Gazette des Hôpitaux*, October 10th, 1879) recommends linear division of the pectoral muscles previous to excision of deeply seated glands. As these glands lie chiefly along the vessels, there is great danger of hemorrhage, and even if the main vein itself is not wounded, some of the large veins going to it may be easily nicked and give rise to free hemorrhage.

In excision of the breast, when the axillary glands are affected they must always be removed, and this is often a difficult operation. The glands are very apt to become adherent to the vessels, especially the vein, which has often been wounded during removal of glandular tumors. When clearing the axilla of diseased glands the fingers will be found more serviceable than any cutting instrument, and infinitely safer. The deep lymphatics of the breast anastomose freely with the lymphatics of the fascia covering the great pectoral muscle and unite with the trunk of the deep lymphatics which go to the axilla. The lymphatics of the pectoral fascia do not anastomose freely with those of the muscle beneath, for the direction of the lymphatic flow is from the muscle to the fascia. Abscess of the axilla, originating in the glands, is not uncommon, the glands most liable to suppurative inflammation being those under the edge of the great pectoral muscle. The course which pus takes when it forms in the axilla has already been described with the fascia. Strumous glands in the axilla frequently break down and suppurate, leaving sinuses which are very difficult to heal.

Supernumerary mammæ have been frequently reported as occurring in the axilla. Dr. Garland (*Edin. Med. Jour.*, 1877) reports cases in which there were swellings in the axilla during pregnancy and suckling; and Dr. Sharpe (*Med. Times and Gazette*, 1855) mentions a case in which a supplementary mamma, which enlarged greatly during pregnancy, occurred in each axilla, and milk could be squeezed out apparently through pores in the skin; there was no appearance of nipples.

Mr. Birkett (*Med. Times and Gazette*, vol. ii., 1868) describes several cases of cystic tumors occurring in early life in the axilla and extending into the neck. He strongly advocates excision in these cases.

Fatty tumors frequently develop in this region; they can be removed without much difficulty.

Francis J. Shepherd.

SIALAGOGUES.—This term is applied to remedies that increase the secretion of saliva. In the normal state of the organism the secretion of saliva is a reflex process excited by chemical and mechanical stimuli. These affect the gustatory nerves and the sensory filaments of the trigeminal and glossopharyngeal nerves of the whole buccal cavity. Such stimuli are all foods and drinks that have a perceptible taste and the mechanical movements necessary in masticating. The stimulating impressions upon the sensory nerves are conveyed by them to the salivary centres, especially to the centre in the medulla oblongata; from these centres impulses are transmitted through the efferent nerves to the salivary glands, and as a result of these impulses there are an increased flow of blood to the glands and an abundant secretion of saliva. Hence it is observed that the saliva is most abundant when food has a very decided and agreeable taste and the process of mastication is slowly and thoroughly performed. In abnormal states of the buccal cavity, especially in the various forms of stomatitis, in consequence of the irritation of the sensory nerves, a more or less abundant flow of saliva takes place reflexly. (See also the article on *Saliva.*)

Most sialagogues act in the same manner as the normal stimuli of the secretion, that is, reflexly; by notably impressing the sensory nerves of the buccal cavity they excite the salivary centres and these transmit impulses to the salivary glands. Hence the greater the stimulating effect of sialagogues upon the sensory nerves of the mouth, the more abundant the salivary secretion. Very pungent substances, such as pellitory, mezereum, cubeb, capsicum, mustard, and ginger, if kept in contact with the buccal mucous membranes for some time, cause a free flow of saliva. Numerous other remedies having a decided action upon the sensory nerves of the buccal cavity, such as vegetable and mineral acids, alkalies, simple bitters and aromatics, ether, chloroform, and alcoholics, reflexly increase the flow of saliva.

Some sialagogues, however, do not act reflexly; they cause a very free flow of saliva when they are injected into the subcutaneous tissue or when they enter the blood by other routes. They act directly upon the peripheral ends of the secretory nerves of the salivary glands, and hence are called remote or specific sialagogues. The principal one of them, and the only one used therapeutically, is pilocarpine; others are physostigmine, muscarine, and nicotine. The preparations of mercury also act specifically; but when they have produced stomatitis the local irritation is necessarily followed by reflex salivation. The preparations of iodine and chlorate of potassium also increase the secretion of saliva by acting upon the secretory nerves.

Sialagogues are used when the salivary secretion is insufficient. This occurs in some persons who eat very rapidly; it is also frequently observed in prolonged febrile diseases, and it is one of the results of poisoning with certain alkaloids and ptomaïnes.

In the dyspepsia of persons eating too hastily sialagogues are probably of little or no benefit; but the adoption of correct habits in eating is generally soon followed by normal digestion. Such patients should be advised to masticate very slowly and at each meal to eat a sufficient amount of hard and dry food, such as stale bread, dry toast, crackers, to excite an abundant flow of saliva. When the teeth have become so defective that food cannot be thoroughly masticated, the patient should be advised to consult a dentist.

The salivary secretion is always diminished in high fevers, and it is sometimes almost completely arrested. When the patient constantly breathes through his mouth, the buccal mucous membrane sometimes becomes so dry that the movements of the tongue, articulation, and deglutition become difficult. In consequence of the dryness, the mucous membrane becomes fissured and abraded, thus presenting numerous openings for the entrance of micro-organisms. Various annoying and dangerous morbid conditions may result, such as soreness, ulceration, and bleeding of the gums, caries of the teeth, fœtor of the breath, glossitis, inflammation of the glands of the neck, of the Eustachian tube and the middle ear. Hence, while sialagogues are used to maintain the secretion of the saliva, all other appropriate means should be employed to prevent the dryness of the mucous membrane. The air of the patient's apartment should be kept moist; the patient should frequently drink water, at least every hour; a piece of wet wide-meshed fabric should be laid over his open mouth; and every three or four hours the entire buccal cavity should be moistened by means of a large camel-hair brush with a mixture of one part of glycerin and two parts of peppermint water. The only sialagogues appropriate in fevers are the acids; of these the most agreeable one is citric acid as contained in lemonade, which has been used from time immemorial as a pleasant drink to quench thirst in high fevers. The other acids that may be used are tartaric, acetic, phosphoric, and hydrochloric, very much diluted and given at short intervals. Some authors hold that only vegetable acids should be given, because they do not, like the mineral acids, diminish the alkalinity of the blood, which, according to some researches, always becomes diminished in prolonged fevers; others are of the opinion that the mineral acids deserve preference because they do not increase oxidation.

The buccal mucous membrane becomes intensely dry from arrested secretion of saliva and mucus in poisoning with belladonna, hyoscyamus, and stramonium, and to a somewhat less degree in poisoning with decayed meat, fish, and cheese. The arrested salivary secretion is, of course, only one of the symptoms; but it may be abated and some of the other symptoms allayed by the cautious administration of pilocarpine.

Pungent sialagogues have been used to allay toothache, earache, and other congestive and inflammatory affections of the nose, ear, and other parts of the head. During the profuse flow of saliva excited by their mastication, the salivary glands are very abundantly supplied with blood, and doubtless this hyperæmia may lessen the flow of blood to adjacent parts of the head and be of some benefit. For this purpose pyrethrum was generally preferred.

Samuel Nickles.

SIDE-CHAIN THEORY OF PAUL EHRLICH.—(Synonyms: Lateral-chain theory; Receptor theory. German, *Seitenkettentheorie*; French *Théorie des chaînes latérales.*)

DEFINITION.—An hypothesis which attempts to explain according to chemical laws the mechanism of the processes of infection and immunity.

The side-chain theory first appeared as an explanation of the mechanism of the assimilation of foods (Ehrlich, Paul: "Das Sauerstoffbedürfniss des Organismus," 1885). According to this hypothesis a food must become chemically bound to a cell in order to be assimilated. Union of food and cell depends upon chemical structure. No matter what may be the chemical structure of a food, it must at least contain a chemical group which allows it to unite with a cell. This chemical group in a food is its "binding group" or "haptophorous group" (from the

Greek ἅπτειν, to bind to). The cell also must contain a binding group or haptophorous group with chemical affinity for the corresponding group of the food. When a food in the circulation passes near the cell, the chemical affinity between the haptophorous group of the cell and that of the food leads to the withdrawal of the food from the circulation and to the chemical union of the food and cell by means of their mutually attractive haptophorous groups. When thus chemically bound to the cell the food can be elaborated into an integral part of the cell, or it can be used up and thrown off as waste products. That portion of the cell which contains the haptophorous group is called by Ehrlich the "side chain" or "lateral chain" or "receptor" of the cell.

Side chain or lateral chain is a term used in chemistry to designate certain substitution products of the benzene ring. The term is used by Ehrlich to suggest an analogous condition in the cell. Receptor simply indicates that this portion of the cell "receives" the food or other material to be mentioned later.

Ehrlich supposes that a cell is composed of two parts: the side chains and the "Leistungskern" or "Central Group." The central group consists of a great number of complicated molecules whose interaction upon each other and upon the foodstuffs is the chemical basis for all vital phenomena manifested by the cell. The special function of the side chain is to bring food to the cell. Each cell possesses a number of different side chains with affinities for different foods, and, furthermore, at least some of the side chains of one cell differ from the side chains of other cells.

This theory of assimilation was first adopted by Ehrlich in 1897 as an explanation of the mechanism of infection by soluble toxins, such as diphtheria and tetanus, and of antitoxin formation (Ehrlich, Paul: "Die Wertbemessung des Diphtherieheilserums," etc. "Klinisches Jahrbuch," 1897). A little later he extended the theory to explain the mechanism of bactericidal immunity and also to account for all those reaction products which are known as cytotoxins, cytolysins, agglutinins, precipitins, coagulins, etc.

The explanation of infection and immunity is simple if one remembers Ehrlich's assimilation theory. If a toxin such as tetanus toxin is injected into an animal the toxin causes no injury unless it becomes chemically united to some vital cells of the animal. If such union does occur it means that the toxin chances to possess a binding group or haptophorous group with affinity for a corresponding haptophorous group or side chain of the cell. Only after union between the cell and toxin by means of their corresponding groups can the specific action of the toxin be directed against the cell.

Ehrlich assumes that the toxin consists of two parts. One, the haptophorous or binding group, happens to resemble the haptophorous group of some normal foodstuff so closely that it can unite with the side chain of some of the body cells. The second part of the toxin is the specific functioning part. This Ehrlich calls the "toxophorous group" of the toxin. These groups may be independent of each other. Either group may be injured without affecting the other. Ehrlich obtained evidence that the toxophorous group is actually less stable than the haptophorous group. Under various conditions a toxin may lose its power of producing the symptoms of poisoning, while it still possesses its power of uniting. Such a toxin Ehrlich called a "toxoid," that is, a "toxin-like" body. A toxoid is a toxin whose toxophorous group is destroyed while its haptophorous group remains intact.

If a dose of toxin is injected into a naturally immune animal the result is negative, for the toxin finds no side chains with affinity for its haptophorous group. In other words, the toxin is unable to unite with any cells of the experimental animal and one fundamental prerequisite of intoxication is absent.

If, however, the toxin is injected into a susceptible animal, the toxin molecules become bound by the haptophorous groups to the corresponding side chains of the cell, and thereupon the toxophorous group of the toxin acts upon the central group of the cell to produce the phenomena of the specific disease. If the virulence of the toxin is great the animal dies; that is to say, if the chemical energy of the toxophorous group is great, the central groups of the cells of vital organs are injured and thrown out of function and the death of the animal results.

But the toxin may be less virulent. The toxophorous group may have such little energy that the central groups of the cells of the animal are not thrown out of function. In this case the toxin is anchored to the side chain of the cell by means of the haptophorous group, and the toxophorous group causes little injury to the cell. The cell then functions normally except that the side chain occupied by toxin is not free to pick up food. The toxin remains attached to the side chain, for not being a foodstuff it cannot be digested and thus removed from the side chain. The side chain thus occupied by toxin is a useless encumbrance to the cell and is accordingly removed as if it were a foreign body, the combined toxin and side chain being thrown off as a waste product.

But the cell requires just such a side chain for the normal process of assimilation. Therefore the cell repairs the defect caused by the loss of its side chain by forming a new side chain whose properties are identical with those of the one that was thrown off.

According to a law formulated by Weigert, tissue formed to repair a defect tends to be formed in excess of the original tissue lost. Ehrlich applies this law to the repair of the side chains and supposes that whereas possibly one side chain is lost, several or many side chains are formed to replace it.

But the cell requires only one such side chain under normal conditions, and all more than one are superfluous. The superfluous side chains are really encumbrances to the cell and are thrown off as waste products.

It is seen that these side chains arise to repair the defect caused by the loss of a pre-existing side chain. The pre-existing side chain was distinguished by having a chemical affinity for a certain foodstuff, and chanced to have the same affinity for a toxin. The newly formed side chains being identical with the ones which pre-existed must, therefore, have the same chemical affinity for the same foodstuff and same toxin.

Such side chains, formed as reaction products of the cell to the toxin and thrown off into the circulation, are the antitoxins. Of course the side chains thrown off into the circulation still retain their affinity for the foodstuff and for the toxin. Enormous amounts of such free side chains or antitoxins may accumulate in the plasma of an animal which then possesses a high degree of antitoxin immunity. If toxin is injected into such an animal, it is picked up at once by the circulating free side chains or antitoxins, union occurring between the mutually attractive haptophorous groups of the toxin and antitoxin. The toxin is thus rendered innocuous, for the means is removed by which it could otherwise unite with the body cells. It is seen that the antitoxin does not necessarily destroy the toxin, but simply neutralizes it by blocking its haptophorous group.

Serum taken from such an immune animal and injected into a susceptible animal confers a temporary immunity (passive immunity) upon the second animal, the mode of action being the same that has just been described. The antitoxic serum must be injected before the toxin has become anchored to the body cells. Otherwise enormous doses of antitoxin are needed and the result is even then uncertain.

Evidently the affinity between the side chain of the cell and the haptophorous group of the toxin is specific, and specific in a chemical, not a biological sense. That is to say, the side chain will not unite with any substance which has not an affinity for the haptophorous group of the side chain, but will unite with any substance possessing such an affinity, whether it be foodstuff, toxin, or other material.

Each cell contains a number of different side chains with affinities for different food materials in the circulation. While one or two side chains of a cell are concerned in the process of intoxication and antitoxin formation, the rest continue to function normally.

Ehrlich's theory explains readily the origin and mode of action of the cytolysins, agglutinins, etc.

If an animal be treated with inoculations of bacteria in doses less than fatal, the serum of the animal acquires several new properties.

If a few drops of the serum are added to a few drops of suspension of bacteria of the species injected, the bacteria lose their motility and collect in clumps and balls, that is to say, they become "agglutinated." Those substances in the serum which produce agglutination are termed "agglutinins."

The serum of the inoculated animal frequently shows another new property. If a few drops of the serum are added to a culture of the bacterium in fluid medium some products of bacterial action dissolved in the liquid are precipitated from solution. These substances in the serum which cause such a precipitation are called "precipitins."

Frequently the serum of the inoculated animal acquires the power of completely dissolving the bacteria. Such a serum is called a "bacteriolytic" serum. The substances in the serum which cause the dissolution of the bacteria are called "bacteriolysins," or less strictly "lysins." The process of disintegration of the bacteria is called "bacteriolysis" or simply "lysis."

The process of bacteriolysis was first described by R. Pfeiffer, and is known as "Pfeiffer's phenomenon." Several valuable additions were made to Pfeiffer's description by Metschnikoff and Bordet. The most important discovery was made by Bordet, who found that it is just as easy to immunize animals against other cells as against bacteria. Bordet inoculated guinea-pigs with the red blood corpuscles of rabbits, and found that the serum of the guinea-pig acquired the power of agglutinating and also of dissolving the corpuscles of the rabbit. These observations have been extended so that now it can be stated as a general law "that the serum of an individual of species A, which has been treated with . . . inoculations of the erythrocytes of species B acquires new properties which enable it to dissolve the erythrocytes of species B" (Sachs, Lubarsch-Ostertag, vii. Jahrgang).

The substances in the serum which cause the dissolution of the red corpuscles are called "hæmolysins"; the serum is "hæmolytic," the process is "hæmolysis."

It is possible to produce sera which will dissolve other cells also. In the literature of the day one finds accounts of "leucolysins," sera which dissolve leucocytes; "nephrolysins," sera which dissolve kidney cells; "hepatolysins," sera which dissolve liver cells, etc.

In the same way there can be produced "hæmoagglutinins," etc.

"Precipitins' can be formed by inoculating one animal with the serum of another. "Coagulins" have been produced by inoculating one animal with the milk of another.

An animal is said to be "immunized" when it is treated with inoculations, whether of toxins, bacteria, red blood corpuscles, serum, or any other material, and the animal thus treated is spoken of as an "immune" animal. Thus a guinea-pig can be immunized against cholera vibrios, the guinea-pig's serum dissolving the vibrios. The guinea-pig can be immunized against typhoid bacilli, the serum agglutinating the bacilli. A rabbit can be immunized against human serum, the serum of the immune rabbit producing a precipitate in human serum. The goat can be immunized against the red blood corpuscles of the ox, the serum of the immune goat producing lysis of the red blood corpuscles of the ox, and so on.

In all such cases the serum of the immune animal becomes toxic for the species from which material was taken for inoculation. In the last case mentioned the serum of the immune goat is toxic for oxen. A serum which is toxic for the cells of another animal is called a "cytotoxin," though of course cytotoxin includes all other cell toxins also. The general name for the process of dissolution of cells is "cytolysis." Sera which cause the dissolution are "cytolysins," though of course any other substance which produces solution of cells is a cytolysin also. All of these reaction products in the serum of an immunized animal appear to have their energies especially directed against material like that with which the animal was inoculated; hence these reaction products are termed "antibodies."

Much information concerning the process of cytolysis, especially of hæmolysis, has been furnished in recent years by the investigations of Ehrlich and his pupils (see particularly the works of Ehrlich, Morgenroth, and Sachs). In their first researches Ehrlich and Morgenroth worked with the serum of a goat which had been immunized against the red blood corpuscles of a sheep, the goat's serum, therefore, dissolving the red blood corpuscles of the sheep. Subsequently, a great number of different combinations was employed. Ehrlich and Morgenroth corroborated Pfeiffer and Bordet in their conclusion that there are two substances in the serum concerned in producing cytolysis. One of these substances appeared as the result of inoculating or immunizing the animal. It was, therefore, called the "immune body."

Ehrlich and Morgenroth found that the immune body in the serum of the immunized goat readily unites with the red blood corpuscles of sheep. This immune body by itself, however, even when united to the corpuscles of the sheep, produced no change in them. The lysis of the red blood corpuscles resulted only when a second constituent of the serum was added. This substance was, therefore, called "complement," because it completed the action of the immune body.

The immune body was a new constituent of the goat's serum which first appeared after the goat had been inoculated with red blood corpuscles of the sheep. The immune body was quite a stable body with marked resistance to heat, light, and chemical reagents. It possessed the property of uniting with the red blood corpuscles of sheep. This union occurred quickly and even at low temperatures. The immune body had an affinity for the red blood corpuscles of sheep which was specific. This specificity, it was found, was of a chemical nature, as described above. The distinguishing feature of immune body was that when immune body, complement, and red blood corpuscles of sheep were brought together at a suitable temperature (about 37° C.) lysis of the red blood corpuscles resulted.

The complement was a normal constituent of the goat's serum, being neither increased nor diminished by the inoculations with corpuscles of sheep. The complement occurred in normal goats which had not been inoculated. It was also found in the serum of normal sheep and of other normal animals. Complement was a very unstable body with little resistance to heat, light, and chemical reagents. It could not be made to unite directly with red blood corpuscles. Only after the immune body had united with the sheep's corpuscles was it possible to bring about union of the complement, and even then union would not occur at low temperatures. The distinguishing feature of complement was that when complement, immune body, and the red blood corpuscles of sheep were brought together at a suitable temperature, lysis of the red blood corpuscles was produced.

Ehrlich was able to explain in terms of the side-chain theory the various phenomena manifested by the antibodies mentioned in the outline just given. He concluded that there must be several forms of side chain. The simplest form is a side chain whose only function is to unite with the foodstuff, thus bringing the food within reach of the central group of the cell. This form of side chain has been considered at length in describing the side-chain theory of assimilation and of antitoxin immunity.

A second form of side chain is so constructed that it not only unites with the foodstuff but also exerts a cer-

tain digestive or enzyme-like action upon it before the central group comes into play. This type of side chain contains two chemical groups: the haptophorous group and the zymophorous or enzyme-like group.

If any inoculated material happens to have an affinity for an haptophorous group of such side chains union occurs. The side chain is thrown off from the cell, new formation, overproduction and setting free of side chains follow according to the requirements of the side-chain theory. The side chains set free in the circulation being identical with the pre-existing side chain, are characterized by having both an haptophorous and a zymophorous group. When such a free side chain or antibody encounters material for which it has an affinity, in the first place, union occurs between the mutually attractive groups, and then the zymophorous group of the side chain exerts its action upon the material.

Agglutinins and coagulins are to be classed as free side chains or antibodies of this order, for they not only unite with substances for which they have an affinity, but also produce definite changes in those substances.

A third type of side chain remains to be considered. Here the side chain possesses both a haptophorous group with affinity for some foodstuff and also a second binding group with affinity for an enzyme-like substance in the circulation. Suitable food molecules unite with the haptophorous group of these side chains, whereupon the second binding group picks up the enzyme-like substance for which it has an affinity, and changes are brought about in the food by this enzyme-like substance.

If inoculated material happens to have an affinity for the haptophorous group of such side chains, union occurs, the side chains are thrown off, new formation and overproduction follow, and the new side chains are set free in the circulation. The free side chains or antibodies, being like the pre-existing side chains, are capable of uniting with two substances: first, the inoculated material; the other, the enzyme-like substance in the serum of the immune animal.

If such a free side chain or antibody encounters material for which it has an affinity, union occurs between the mutually attractive groups, and then the second binding group of the antibody picks up from the circulation the enzyme-like substance, which in turn exerts its action through the antibody upon the inoculated material.

This is the mechanism of cytolysis. The inoculated cells have led to the new formation, overproduction, and setting free in the circulation of certain side chains. These free side chains or antibodies are the immune bodies in the serum of the immunized animal. The enzyme-like substance normally present in the serum of the animal is the complement. If some cells of the sort inoculated are treated with serum of the immunized animal under proper conditions the immune body unites with the cells, the complement unites with the immune body, and lysis of the cells results.

It is not yet definitely settled whether precipitins are antibodies of the second order like agglutinins, or of the third order like cytolysins. Recent investigations indicate that the precipitins are antibodies of the third order.

These three types of side chain suffice to account for all the reaction products thus far investigated. There are many features of the side-chain theory which cannot be entered into in this review. In general it may be said that the chemist's point of view has been adhered to by Ehrlich in dealing with all the complicated phenomena met with in studies in immunity. From what has been said it is evident that the prerequisites of antibody formation are few—a substance inoculated into an animal must possess a chemical group (the haptophorous group) which will unite with the side chain of some cell of the animal. If the cell is not injured and if the inoculated substance is not removed by digestion by the central group, conditions are favorable for antibody formation.

Several other antibodies are known in addition to those already mentioned. By inoculating an animal with ferments it has been possible to produce "antiferments" which are of the same type as antitoxins. By inoculating with a serum rich in agglutinins or coagulins it has been possible to produce antibodies which prevent the action of the agglutinin or coagulin. These substances are termed "antiagglutinins" or "anticoagulins." They are really "anti-antibodies." It has also been possible to produce substances which prevent the action of the complement, *i.e.*, "anticomplements" and substances which prevent the action of the immune body, *i.e.*, "anti-immune bodies."

Many of the substances mentioned above, such as agglutinins, cytolysins, anticomplements, etc., have been found in the serum of many normal animals. Such normal antibodies can be readily accounted for as free side chains.

It has been found that the physical and chemical properties of the immune body and of the complement are subject to quite wide variations, and also that there are great numbers of different immune bodies and complements in the serum of any one animal.

Evidence goes to show that the complement arises from cells in the circulation, probably leucocytes. It has been found also that a certain quite definite chemical substance, lecithin, can act as complement.

It has been possible to apply nearly all of the deductions made from studies with hæmolytic sera to the various infectious diseases and to various animal and vegetable poisons.

There seems to be no fundamental antagonism between the side-chain theory of Ehrlich and Metschnikoff's phagocytic theory of immunity.

In concluding it will be well to give a list of other terms used in the literature of immunity. It has been stated that the complement is the unstable enzyme-like material normally found in certain animals. This material is also spoken of as "addiment," "cytase," or "alexin."

The immune body is also called "amboceptor" (that is, receptor with two binding groups), "substance sensibilisatrice," "präparator," "fixateur," "copula," "desmon," "intermediary body," or "Hilfskörper." The anti-immune bodies are also spoken of as "anti-amboceptors."

Harry T. Marshall.

SIDEROSCOPE.—The use of a magnetic needle for detecting foreign magnetic bodies in the eye was first advocated in 1880 by Thomas R. Pooley, of New York, but the suggestion did not attract much attention until the subject was taken up by Edward Asmus in 1894, who utilized the principle in an instrument which he called a *sideroscope*. Since then several modifications of the instrument have been brought forward, but for practical purposes Hirschberg's model is probably the best. This consists essentially of a magnetic needle suspended by a vertical thread, to which is attached a small mirror. The deflections of the needle produced by a foreign body in the eye of a patient is indicated by a beam of light from a lamp which is reflected by the mirror upon a graduated scale. The chief disadvantage of the instrument lies in its instability, for which reason it can be used with success only in places free from vibration. While it is quite delicate, many ophthalmologists claim that it is entirely unnecessary where Haab's giant magnet and an x-ray apparatus are available. *Frederick Herman Verhoeff.*

SIDEROSIS.—Ordinarily this term is used to designate the pigmentation of the lungs produced by the inhalation of any sort of metallic dust, but strictly it should refer to the deposition of iron pigment alone in any of the tissues of the body. A full account of siderosis used in the former sense will be found under *Pneumokoniosis*. True siderosis is usually due to the breaking down of the red corpuscles of the blood, and is best spoken of as *hæmatogenous siderosis*. This takes place to some extent in many chronic diseases, but especially in pernicious anæmia, and involves particularly the liver, spleen, bone marrow, and kidneys. It also occurs as the result of the disintegration of hemorrhages, as is the case, for instance, in chronic passive congestion of the lungs, and not infrequently in tumors. For this reason tumors should al-