PLASMA CELLS.—In 1891 Unna described the elements which he called "plasma cells," believing them to correspond with certain granular connective-tissue cells to which Waldeyer had previously given the same name. Later studies indicated that the two were not identical, and Waldeyer advised the restriction of the term "plasma cell" to that of Unna, finding that the structures named by himself (Waldeyer) corresponded, at least in large part, with the "mast cells" of Ehrlich. Various papers on plasma cells have appeared since Unna's earlier publications, while their nature and properties have been the subject of numerous discussions, often lengthy and occasionally acrimonious. From this it appears that our knowledge of them is still far from definite. There is even some difference of opinion as to what a plasma cell is in fact. It has received its name on account of having *protoplasm* that may be stained by basic aniline dyes. This property is by no means peculiar to it, however, and is shared by several other varieties of cells; for instance, ganglion cells, lymphocytes, osteoblasts, certain giant cells, and mast cells. (In the case of mast cells, large granules contained in the body of the cell are the part stained, and they assume a different shade of color from that of the pure stain itself—metachromism.)

Morphology.—With Unna's polychrome methylene blue (described hereafter) the protoplasm of the plasma cells is stained blue-violet, while the nuclei become blue. The outer part of the protoplasm stains more deeply than the inner part, leaving a pale zone around the nucleus. The nucleus is round or oval, and is usually placed eccentrically. Five to eight deeply stained masses of chromatin occur in the nucleus, chiefly around its border. Some observers have described a nucleolus. Two or more nuclei are occasionally present. In size the plasma cells vary from being of the dimensions of a leucocyte to objects of a much larger size—average diameters, 6 to 7 μ by 8 to 10 μ. In shape they are round, oval, roughly cubical, or elongated, according to whether or not they are confined by connective-tissue fibres or by the pressure of other cells. Evidences of both mitotic and amitotic division have been witnessed in plasma cells.

The above account is, in all essential respects, in accord with the views of von Marschalkó, which have been adopted by the majority of workers. It differs somewhat from the one originally given by Unna. According to Unna, the plasma cells have protoplasm that contains numerous granules capable of being stained. Such granules have not been seen by most other observers. It is not uncommon, however, to find plasma cells whose protoplasm is not homogeneous, but which contain small clumps and particles that stain unequally and irregularly. Cells having the metachromatic granules characteristic of mast cells, but otherwise like ordinary plasma cells, have been seen—plasma mast cells. These are unusual. Furthermore, according to Unna, the nuclei of plasma cells give up their stain much more easily than does the protoplasm, and in a preparation properly made the nuclei appear as unstained spots. Some have even maintained that two kinds of plasma cells exist, those of Unna and those of von Marschalkó. However, it is certain that the staining of the nucleus depends much on the technique employed.

Occurrence.—Although they were at first supposed to belong only to pathological conditions, plasma cells have been reported as occurring in lymph nodes, in the lymphoid tissues of the spleen, and in the bone marrow, both in man and in the lower animals, in ligaments, in the framework of mucous glands of the tongue, and in the mucosa of the stomach and intestine in man. Information as to their distribution in normal tissues is not very full or exact.

On the other hand, so much has been written on their occurrence in diseased conditions that a mere enumeration of these conditions is impracticable. Unna's first accounts of plasma cells were based on sections of lupus. He directed attention to tumor-like collections of these cells. Such a collection he called a "plasmoma." It has since been learned that plasma cells are abundant in the lesions of tuberculosis wherever situated, in those of syphilis, leprosy, actinomycosis, and rhinoscleroma—*i.e.*, the so-called "infectious granulomata." They are also frequently seen in the stroma of carcinoma. In the main they are characteristic of rather chronic processes, where they constitute an important part of what is often termed round-cell infiltration. They are said to collect especially around small arteries. Their relations with the epithelioid cells of granulation tissue are in dispute. In acute inflammatory conditions, and especially in acute suppuration, they appear in smaller numbers. Plasma cells have, however, been demonstrated in acute inflammatory lesions, bacterial or otherwise, in keratitis in the rabbit, in recent granulating wounds in man and in the dog, in the lesions of typhoid fever, in the cell infiltration of acute interstitial nephritis, and in the stroma of the lung and even in the exudate late in lobar pneumonia. Further work is needed on their relations to the cells of sarcomata, and it may possibly yield information of use in diagnosis. The study of the plasma cells in diseases of the skin has been carried on by Unna with great energy; the results may be found in his "Histopathology of the Skin."

Origin and Functions.—Unna held that the plasma cells were derived from connective-tissue cells, stating that he was able to detect all the necessary transitional forms between the two. This theory has obtained a few adherents. Most observers, however, believe that plasma cells are derived from the lymphocytes, and chiefly from the small lymphocytes. It is claimed by some, furthermore, that plasma cells may become connective-tissue cells and thus aid in the formation of fibrous tissue. This latter hypothesis would make the production of connective tissue from lymphocytes possible under certain circumstances, the plasma cells being an intermediate stage. It would modify existing ideas considerably and convincing proofs will be demanded before it can be accepted.

Some writers take a middle ground, believing that the plasma cells come in part from lymphocytes and in part from connective-tissue cells.

The functions of plasma cells in other respects are equally uncertain. It is to be noted that they are not distinctive of any particular disease or class of diseases. Their relative absence in acute suppuration is remarkable. According to Councilman and Mallory, they have the power of amœboid movement, they may occur inside the blood-vessels, and may be seen in the act of emigrating from the blood-vessels. It is doubtful if they possess phagocytic properties, and if so these are probably not energetic.

Other ideas that have been proposed as to their functions are purely speculative. It has been suggested that their peculiar staining property is the expression of diminished activity or degenerative changes, that it indicates an increase of activity, that it is due to their having taken up chromatin from other and degenerated cells, that they have some protective function, and that they serve to eliminate some unknown substance.

Technique.—Fixation of tissues may be secured with alcohol, corrosive sublimate, Zenker's fluid, formaldehyde, or Müller-formol. Either paraffin or celloidin embedding may be used. Various methods for staining plasma cells have been proposed. Unna's alkaline or polychrome methylene blue gives satisfactory results; thionin or toluidin blue serves equally well. The plasma cells may sometimes be stained with hæmatoxylin. The following formula, which is one of many given by Unna, will be found serviceable: Methylene blue, 1 part; potassium carbonate, 1 part; distilled water, 100 parts. The solution must stand for periods varying from weeks to months before it is fit for use.

Stain in the methylene-blue solution, which may or may not be diluted, fifteen minutes or longer. The sections will be overstained.

Rinse in water.

Decolorize in water to which a few drops of "glycerin-ether" have been added, for a quarter of a minute or several minutes, as required, till differentiation of the structure begins to appear (one-per-cent. acetic acid, or alcohol alone serves nearly as well).

Rinse in water.

Complete the decolorization with alcohol.

Clear in oil of bergamot or xylol.

By this process the plasma cells are stained blue-violet, their nuclei and other nuclei and bacteria blue, the granules of mast cells violet to red. Epithelial cells take the blue stain, sometimes intensely, especially the horny layers of the epidermis; giant cells are frequently stained as well; also the products of certain degenerations, as amyloid and mucoid, which may show varying degrees of metachromism. *Herbert U. Williams.*

The literature of this subject up to June, 1900, will be found in an article by the present writer in the American Journal of the Medical Sciences of the same date. The most important articles that have since appeared are the following:
Almkvist: Arch. f. Dermatol. and Syph., Bd. lviii., 1901.
Askanazy: Centralbl. f. allg. Path., etc., Bd. xiii., 1902.
Beattie: Journ. Pathol. and Bacteriol., vol. viii., p. 129.
Bosellini: Soc. Med. Chir., Bologna, December, 1901. Abs. Centralbl. f. allg. Path., etc., Bd. xiii., 1902, p. 331.
Enderlen and Justi: Deutsch. Zeitschr. f. Chir., Bd. lxii., 1901.
Friedländer: Arch. f. klin. Chirurg., Bd. lxvii., 1902.
Harris: Journ. Amer. Med. Assn., vol. xxxviii., 1902, p. 634.
Herbert: Journ. Pathol. and Bacteriol., vol. vii., p. 91.
Mallory: Journ. Exper. Med., vol. v., p. 1.
Pappenheim: Virchow's Arch., Bd. clxv., 1901, clxvi., 1901, clxix., 1902.
Schlesinger: Virchow's Arch., Bd. clxix., 1902.

PLASMODIUM MALARIÆ.—The protozoan parasite which Laveran discovered in 1880 was designated by Marchiafava and Celli Plasmodium malariæ. The organism which is classified with the sporozoa has little resemblance to the multinucleated amœboid bodies to which the term plasmodium has been given by zoologists; but even though unsuitable the binomial name, in virtue of its priority, is applicable to the species to which it was originally given. Observations inaugurated by Golgi have shown the existence of three readily distinguishable varieties of parasite, each of which is capable of producing malarial fever. The organism discovered by Laveran and later studied by Marchiafava and Celli is the æstivo-autumnal parasite which causes the most severe type of intermittent fever, characterized by irregular periodicity and occurring most commonly during the late summer and fall. That type of malarial fever which recurs at regular intervals of two days is caused by a closely related parasite which, nevertheless, presents such well-marked peculiarities that it is usually regarded as a distinct species. A third parasite causes the quartan type of malarial fever, distinguished by paroxysms recurring at intervals of three days. If, in accordance with the opinion of a few observers, it should be shown that the three parasites associated with these various types of fever are varieties of a single species, the name Plasmodium malariæ is applicable to this variable organism. In the present article, however, the organisms associated with tertian, quartan, and æstivo-autumnal malaria will be described as separate species.

The parasites of the malarial fevers multiply within the red blood corpuscles of their human host. Recent research has demonstrated that they are capable of development within the body of certain suctorial insects, which have fed upon the blood of an individual suffering with malarial fever. A second individual is infected by the bite of such an insect, which thus acts as an intermediary host.

Geographical Distribution of the Malarial Parasite.—The general and local conditions which favor the occurrence and spread of malaria are such as conduce to the extracorporeal existence of the parasite. The presence of mosquitos capable of transmitting the organism is essential to the endemic occurrence of the disease, so that the geographical distribution of malaria is in great part dependent upon factors which aid the multiplication of certain species of mosquitos.

In Africa, malaria prevails in its most pernicious form on the west coast, especially in the neighborhood of the Congo and Niger rivers. South of the Congo malarial fevers become infrequent and disappear in the most southern part of the continent. Upper Egypt is free from the disease, which occurs with great severity elsewhere upon the Mediterranean coast.

In Asia malaria is prevalent upon the coast of Asia Minor, Arabia, and near the Persian Gulf. Endemic malaria abounds not only in the basins of the Indus and of the Ganges, but upon the tableland of the Deccan. In many of the East India islands severe malaria prevails, but in the Philippine Islands, though the disease is widely distributed, it is not particularly severe. Pernicious malaria occurs in places near the coast and along the rivers of China, but in Japan the disease is mild and infrequent. Of interest is the almost complete immunity enjoyed by Australia, New Zealand, and the islands of the Pacific.

In Europe malaria prevails in the southern part of Russia, particularly upon the shores of the Black and of the Caspian seas, along the shores of the Danube, and upon the peninsulas bordering the Mediterranean Sea. In Italy well-known seats of endemic infection are the plains and marshes of the western coast, including the Roman Campagna and the Pontine marshes. Here the disease is so prevalent that it has been designated Roman fever, and its frequency and severity in Italy have stimulated much of the investigation which, since the discovery of the malarial parasites, has explained the complicated life history of these organisms. Northern Europe, including the British Isles, is in great part free from malaria, though there is evidence that at an earlier period, particularly in England and in Denmark, it has occurred with severity in regions where it is now almost wholly absent.

In the West Indies, along the northern and eastern coasts of tropical South America, and in Central America malaria exists in its worst form. The disease is common in the southern part of the United States near the Gulf of Mexico and along the Mississippi and its tributaries. It occurs near the Atlantic coast with gradually diminished severity as far north as New York. Elsewhere are a few scattered localities where the disease is of mild type.

Malaria is pre-eminently a disease of tropical and subtropical countries, but prevails with diminished severity in many parts of the temperate zone. It is endemic in certain localities, particularly near the mouths and along the banks of rivers. In such localities are found the pernicious types of fever caused by the æstivo-autumnal parasite, while where the disease is less prevalent milder types, the regularly intermittent tertian and quartan fevers, are more common.

Conditions which Favor the Occurrence of Malaria.—The influence of temperature upon the occurrence of the malarial fevers is well illustrated by the preceding account of its distribution. In the endemic foci of the tropical and subtropical countries where malaria occurs in its severest form the disease prevails throughout the year. In the temperate zone as the poles are approached its frequency and severity progressively diminish with the temperature, and, according to Hirsch, malarial fever does not occur in localities where the mean summer temperature is below 15° or 16° C. Even in tropical countries its prevalence increases during the summer and reaches a maximum about the beginning of autumn. In temperate regions the disease may be limited to the warmer months of the year. The incidence of the disease in Baltimore, as described by Thayer, illustrates this condition. During January and February malarial fevers are almost absent, but the gradually increasing number of cases which occur during the spring and early summer are of the milder tertian and quartan type. Double tertian and triple quartan infections occur later in the summer, and the æstivo-autumnal parasite makes its appearance. Cases of æstivo-autumnal infection now increasing in number form a very large proportion of those which occur during September and October, and then,