spread of measles in such a room. It does control measles to a large extent, however. This explanation is made to make clear what is meant by partial exposure.

Shirarina C., aged 16 months (referred to above in Group 1), had been given convalescent serum, May 11. May 25, while in another unit, she was partially exposed to a child with a measles rash for about ten hours. Again, June 16, she was partially exposed in the same ward to a second child, who developed a rash, June 16. Shirarina C. did not develop measles, although she had received only the one dose of convalescent serum, May 11.

Howard D., aged 18 months, was partially exposed to a child who developed a measles rash in the same room, May 24, but not in the same unit. This exposure was over a period of several hours. Howard D. was given 10 c.c. of convalescent serum, May 27, taken from five patients nine, four, four, fourteen and six days, respectively, after the rash. Howard D. did not develop measles. Again, June 16, Howard D. was partially exposed to a second patient in the same room, but a different unit. Howard D. was not given any more serum and did not develop measles.

In the same room, in Ward D, June 16, Ralph L., aged 7 years, developed a measles rash. In this room, but in a separate unit, were three children who had not had measles.

Regina C., aged 1 year, and Camella B., aged 2 years, were also patients. The first was given 7 c.c. and the second 10 c.c. of mixed serum, June 16, taken from four patients seven, seven, nine and forty days, respectively, after the onset of the rash. Dorothy G., aged 7 years, on the same day was given 10 c.c. of serum, taken from five patients thirty-one, nine, forty, five and five days, respectively, after the onset of the rash. These three children did not develop measles.

ACTIVE IMMUNIZATION

Three patients were treated as follows:

EXPERIMENT 1.—Esther V., aged 4 years, was partially exposed to a child who, May 24, developed a measles rash in the same room, but in a separate unit for several hours. May 27, she was given 15 c.c. of convalescent serum, taken from three patients five, eight and ten days, respectively, after the rash. On the same day (May 27), direct swabs from the nose and throat of two children, who developed the rash on the same day (May 27), were taken. They were put back into the test tube, and were taken directly to the ward where Esther V. was then a patient. The nose and throat of Esther V. were thoroughly swabbed with this fresh secretion. The time between taking the secretions and the swabbing of the second patient was not over three or four minutes. Esther V. had pertussis and usually had a temperature of about 100. Twelve days later, a discrete hemorrhagic eruption appeared on her face, with a few scattered patches on her body. They were raised to the touch. They were most numerous on her face. On the same evening, the temperature rose to 103. Next day, subsequently, it remained as usual. The rash did not extend, and faded away in a few days. There were no Koplik spots or catarrhal symptoms, and the child sat up in bed as usual, not seeming to be at all ill.

This experiment seems to show that, if she was really infected, either naturally or artificially, and we have reason to believe she was, this patient did, twelve days after inoculation, show a reaction which may have been an abortive measles. If it was an abortive measles, even though the serum did not entirely prevent it, it showed inhibitive power. The reaction might have been due to the serum, but it was not like any I have ever seen.

The attack would never have been thought of as measles unless we had known of the inoculation.

EXPERIMENT 2.—August 11, Regina C., aged 1 year, and Morris S., aged 4 years, neither of whom had ever had measles, were infected with nasal and throat swabbings taken

from a child whose rash began on the day before. Swabs were used on the donor, one of the nose and nasopharynx, and one of the throat. There was only an interval of two or three minutes before the inoculation was done. Both swabs were used in swabbing the nose and throat of the two children, Regina C. and Morris S.

August 12, each child was given 25 c.c. of a mixed convalescent serum, and this was repeated, August 14. The mixed serum was about 2 months old and was taken from eight patients five, six, eleven, nine, eight, seven, ten and nine days, respectively, after the rash. There was no reaction from the serum, and neither child showed any signs of measles in the hospital.

CONCLUSIONS

Six children were definitely exposed to measles and were apparently protected from the disease by immune serum; one, used as a control, developed measles. Eight others were partially exposed and did not develop the disease after immunization. Three other patients received virus inoculation and immune serum simultaneously. In two there was no reaction. In the third there was a slight reaction indicated by a transient rise in temperature and an atypical rash.

The experiments are too few to be conclusive, but they are sufficiently suggestive to warrant further investigation.

THE RELATION OF THE LYMPHOCYTE TO CANCER

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AUGUSTA, MAINE

While the morphology of the various formed elements of the blood is now on a fairly scientific basis, there remains considerable lack of knowledge in regard to the origin and function of these cells. It is a matter of common agreement that the red cells are formed in the bone-marrow in adults and in the liver and spleen in embryos, while the origin of platelets is still in doubt. The polymorphonuclear leukocytes come originally from bone-marrow; the lymphocytes are derived from lymph glands and from tissue, and the large mononuclears have either the same origin as lymphocytes, or develop from endothelial cells lining blood or lymph vessels.

Not all the functions of these cells have been elucidated, although the evidence indicates that the red cells are concerned chiefly in tissue respiration, or the carriage of oxygen to the tissues; while the blood platelets are apparently involved in the phenomena of blood clotting. The white cells as a class are regarded as protectors of the body tissues against injurious agents of all kinds, and are intimately associated with the processes of inflammation. Polymorphonuclear leukocytes and large mononuclears are more involved in the defense of the body through an actual attack against the injurious agents, resulting in the engulfing (phagocytosis), neutralization and absorption of such agents. My opinion is that the small mononuclears, or lymphocytes, which are made up chiefly of nuclear material, have as their chief physiologic function the carriage in the form of nuclear enzymes of energy that is required by normal living body cells in the processes of growth and multiplication. Under abnormal conditions, and in concentrated numbers, these lymphocytes may give additional aid and energy to the normal body cells surrounding areas of injury and inflammation,

thus causing a local speeding up of proliferation and repair.

In the growing embryo, the red cells apparently are the first to appear in the blood, which might be expected if cell and tissue respiration or oxidation is the prime factor in life. Of the white cells, the first to appear in the blood of the young embryo (usually about the tenth week of life) is a cell corresponding to the lymphocyte. Here again it is only logical that the cell which possibly has to do so much with growth energy should appear before the polymorphonuclear cell which has to do with the protection of that growth and life against injury.

During the entire fetal life, which involves characteristically rapid growth and multiplication of body cells and tissues, the lymphocytes remain the most numerous of the white cells; indeed, a relative increase or lymphocytosis persists during early childhood, the period of continuously rapid growth. At the time when body growth has reached its maximum, a definite change is found in the relative number of white cells in the blood, the number of lymphocytes being very much less than that of the polymorphonuclears, while at the same time the special auxiliary lymphoid tissues (such as the thymus) which have to do with growth rapidly atrophy.

It appears, therefore, that the lymphocyte possibly may be described as the male cell of the blood, and that through a process which is as yet not thoroughly understood, it has the power by means of the enzymes of its mass of nuclear material to energize the body cells with which it comes in contact, causing them to grow and divide. It is probable that the lymphocyte, or its energy substance, is under the constant control of an antibody, and that under normal conditions the influence of the lymphocyte and its enzymes is regulated for the exact demands of the body cells and tissues in their regular growth and division, or to meet the special requirements of increased local repair at points of injury.

It is my belief that as the controlled lymphocyte may be the potential father of normal body cells, so the uncontrolled lymphocyte may be the potential father of the tumor cell. The potential mothers of tumor cells are the epithelial cell, the connective tissue cell, the muscle cell or other tissue cells. The offspring of such unions may be the tumor cells themselves—the cancer cell, the sarcoma cell, the myoma cell.

The primary basis of cancer probably is a cell or tissue injury due to various physical, chemical, parasitical, mechanical or metabolic agents. The actions of such agents may be just as certain, even though they are not seen and appreciated. Because there is no history of cell or tissue injury is no reason to doubt this important precancerous factor.

Local injury is followed by local inflammation, and the latter involves the concentration of defensive polymorphonuclears and large mononuclears which attack the agents of injury, and also involves the concentration of the offensive lymphocytes with their energy-bearing enzymes, which may stimulate the surrounding tissue cells to more rapid proliferation and repair. It is significant that the lymphocytes are usually more concentrated at the periphery of a lesion. They are apparently more in contact with and more concerned in the repair work of surrounding tissue cells than in the attack on injurious agents; that is, they are seldom, if ever, phagocytic. These fundamental principles of

my theory in regard to malignancy have been outlined in previous articles on the subject.¹

In the warfare between injurious agents (especially bacteria) and body cells, the polymorphonuclear leukocytes making up the standing army rush to the defense of the body at the point of attack, and by an offensive campaign either destroy the invaders or are themselves destroyed. The endothelial leukocytes constitute the ambulance corps and bear away dead or injured bacteria, polymorphonuclears or other blood cells. The lymphocytes, on the other hand, make up the army of reconstruction. If the repair is of a normal nature, well controlled by antibodies, the result is normal healing. If the repair is of an abnormal nature due to the lack of controlling forces or antibodies, the result is lawless repair or cancer.

Thus cancer may be due to two factors, one local, the other general—a local cell stimulus which is set up by the energy-bearing lymphocytes concentrated by any form of local injury (usually chronic); and a general loss of lymphocytic control due to an acquired or possibly hereditary lack of antibodies in the tissues or circulation. Hence, cancer may be the result of an autoparasitism, in which local accumulations of uncontrolled lymphocytes are the important factors. The prevention and cure of cancer possibly may be brought about by the active or passive increase of the controlling lymphocytic antibodies.

That there is evidence from the work of various investigators to strengthen this hypothesis is indicated by a study of the literature on the subject.

Virchow² was probably the first to suggest an analogy between the fertilization of the ovum and the development of the cancer cell. Klebs³ called attention to the common association of leukocytes and cancer cells, and believed that the former might fertilize epithelial cells and cause the latter to develop into cancer. In a study of resistance against transplanted mouse cancer, Bashford⁴ found that the injection of normal mouse blood corpuscles induced a definite resistance against transplanted cancer. It is possible that corpuscular antienzymes were thus stimulated, with the result that the cancer cells could not find proper energy soil for their development.

Lewin⁵ in like manner, produced resistance against both rat carcinoma and rat sarcoma by the injection of normal rat blood; while Weidanz⁶ obtained somewhat similar results with normal blood inoculations. Apolant⁷ reported induced resistance by the injection of normal blood even from alien species. DaFano⁸ associated the lymphocyte with the distribution, or stimulation, of immunity against transplanted cancer. Bashford, Murray and Cramer⁹ showed that active resistance in mice against transplanted cancer might be developed as soon as four days after the inoculation of normal mouse blood, but that the resistance was greater after ten days—evidence of the stimulation of antibodies. Bashford, Murray and Haaland¹⁰ demonstrated that as high a degree of immunity could be

1. Bristol, L. D.: *Med. Rec.* **83**: 787 (May 3) 1913; *J. M. Res.* **32**: 475 (July) 1915; *Med. Rec.* **89**: 180 (Jan. 29) 1916; *Science* **54**: 58 (July 14) 1916; *J. Maine Med. Assn.* **9**: 57 (Oct.) 1918.
2. Virchow: *Die krankhaften Geschwülste*, Berlin, **1**: 87, 1863.
3. Klebs: *Die allgemeine Pathologie*, Jena, **2**: 524, 1889.
4. Bashford: *Brit. M. J.* **2**: 209, 1906.
5. Lewin: *Berl. klin. Wchnschr.* **44**: 1606, 1907.
6. Weidanz: *Arb. a. d. k. Gsndtsamte.* **30**: 443, 1909.
7. Apolant: *Ztschr. f. allg. Physiol.* **9**: 91, 1909.
8. DaFano: *Ztschr. f. Immunol. Orig.* **5**: 68, 1910.
9. Bashford, Murray and Cramer: *Proc. Roy. Soc., Series B* **79**: 180, 1907.
10. Bashford, Murray and Haaland: *Third Sc. Rep., Imp. Cancer Res. Fund*, London, pp. 395, 369, 1908.

established by inoculation of normal blood as by injection of blood from tumor-resistant mice.

Collection and concentration of lymphocytes are very commonly found around growing spontaneous tumors and around living tumor grafts. DaFano¹¹ believes that in the latter the lymphocytes are concerned with the development of resistance against such grafts. Murphy and his co-workers¹² have shown that mice in which lymph glands and lymphoid organs have been unfavorably affected by roentgen-ray treatment are especially susceptible to the growth of transplanted tumors, and they believe that the lymphocyte is a potent factor in establishing the immunity of mice to transplanted cancer. More recently Murphy and Sturm¹³ have demonstrated that after stimulation of lymphoid elements by heat, tumor grafts are much less successful. Corson-White,¹⁴ in a study of the blood of tumor rats, following cancer-stimulating and cancer-inhibiting diets, found no change in the counts of red cells and no change in the numerical counts of white cells, except in the case of lymphocytes, and here definite changes in their numbers were noted.

One of the most striking and characteristic, as well as fatal, features of cancer is the spread of metastases, usually through lymph spaces and glands, less frequently through the blood stream. Instead of encountering resistance in lymph glands, cancer cells apparently find in lymph cells and tissues a lack of resistance or a definite nutritive soil and extra supply of energy for their continued growth and uncontrolled multiplication.

May we not say of metastatic cancer cells in lymph glands what Herbert Spencer¹⁵ said of plants and animals in general? "The multiplication of any kind of plant or animal in localities that are favorable to it, is a growth where the antagonistic forces are less than elsewhere." What an important step it would be in the solution of the cancer problem if it were possible to control the spread of metastases by causing lymph glands to be actually antagonistic to cancer cells!

It is a significant fact that roentgen rays have an apparently specific effect on cancer cells, spermatozoa, ova and lymphocytes. Their effect on blood corpuscles other than lymphocytes is not marked. Does this not indicate a similarity in the basic substances or energy of such cells?

Based on this theory of the relation of localized uncontrolled lymphocytes and their nuclear enzymes to the energizing of epithelial cells leading to lawless reproduction, or cancer, experiments are being carried on in our laboratory to determine a possible means of controlling lymphocytes and cancer. These experiments will be described in a subsequent communication.

11. DaFano: *Ztschr. f. Immunol. Orig.* 5:1, 1910.

12. Murphy, J. B., and Taylor, H. D.: *J. Exper. M.* 28:1 (July 1) 1918.

13. Murphy, J. B., and Sturm, Ernest: *J. Exper. M.* 29:25 (Jan. 1) 1919.

14. Corson-White: *Proc. Med. Soc. of Penn.*, 1918.

15. Spencer: *First Principles*, New York, D. Appleton & Co., 1896, p. 234.

Racial Factors in Tuberculosis.—The findings in the Framingham demonstration as to racial factors bear out previous experience elsewhere, namely, that the Italian race stock presents a low tuberculosis incidence, in contrast to high rates in French-Canadians, Irish and other race stocks. On the other hand, the von Pirquet skin reaction among children shows a high percentage of infection among Italian children, with a correspondingly low incidence of active disease.—*Bulletin*, National Tuberculosis Association.

THE NEEDS OF MEDICAL EDUCATION AS REVEALED BY THE WAR *

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It is regretted that accurate statistical data to support statements made herein are not yet available, but lack of time as yet has made impossible the analysis of the vast amount of data in the records of the Surgeon-General's Office pertaining to this subject. But the Surgeon-General's great interest in this matter will doubtless result in a critical study of the data and a presentation of the results at no distant date. I do not comment further with respect to the probable results of this future statistical study other than to venture the conviction that they will prove disconcerting to any who may have entertained the idea that general standards of medical education in this country have reached a satisfactory degree of excellence.

You are accordingly asked to consider the following remarks as merely suggestive, as preliminary to the exact information later to be available, and as only embodying general impressions that I gained of medical officers under instruction at medical officers' training camps while I was in general charge of Medical Department training from May, 1917, to May, 1918. During this period I made frequent visits to the several camps located at Fort Benjamin Harrison, Ind.; Fort Riley, Kan.; Fort Oglethorpe, Ga., and Allentown, Pa. The camp at Fort Des Moines, Iowa, was also an instruction center and was duly visited, but was for colored medical officers only.

While accurate figures are lacking, it is doubtless true that more than half the medical officers who entered the service passed through the above named camps. The impressions gained were largely derived, of course, from the commandants of these camps and other officers pertaining to their respective staffs of instructors. They were accordingly second hand to a very considerable extent, but had the advantage of representing the composite ideas of large numbers of instructors.

For the period from May to October, 1918, I was in command of Camp Greenleaf, Fort Oglethorpe, Ga., and consequently was in close contact with the medical officers sent for instruction there. Camp Greenleaf at that time was handling over four fifths of medical officers sent to camps for training, as the camps at Fort Benjamin Harrison and Fort Des Moines had been discontinued, and those at Fort Riley and Allentown greatly cut down. Camp Greenleaf had then some 2,500 officers under instruction at one time, of which over 2,000 were medical officers and the remainder were student officers of the Dental, Veterinary and Sanitary Corps. With the concentration of training, these officers came to Camp Greenleaf from every part of the United States, so that they represented a fair cross section of the medical profession of the country, as it was accepted for service in the Medical Corps of the army.

In this connection, I would say that the opinions of Col. W. N. Bispham, Medical Corps, who will doubtless discuss this paper, should be of equal or greater

* Read before the Fifteenth Annual Conference of the Council on Medical Education of the American Medical Association, Chicago, March 3, 1919.