I should like to complement the members of this conference on the highly critical nature of their reviews and their insistence on quantitative methods and adequate controls in the papers that they have presented.

I came here rather pessimistic about the possible role of immunology in cancer after reading the critical papers by Kidd, Everson, Cole and Southam. It seemed very clear that cases of real regression and disappearance of autochthonous cancer are few, and, when they occur, there is no proof that they result from immunologic mechanisms. Similarly, Southam’s review emphasized the fact that no effective treatment by immunological means has been recorded. I feel more optimistic now after hearing the various discussions.

What are some of the possible developments of the future?

First of all, we are agreed that the occurrence of tumor-specific antigens is central to the use of specific immunologic methods in the diagnosis and treatment of cancer. Assuming the presence of tumor-specific antigens and immunologic mechanisms that suppress the tumors, it is necessary to separate from the tumor-specific antigens those that are actually functional in the immune reaction. Whether or not they are functional depends probably on their location. It is small wonder that this type of work has progressed so slowly. Many of our studies on infectious agents, in which we knew to begin with that immune phenomena operated, progressed very slowly.

An excellent beginning has been made in the various studies of the antigenic properties of the abnormal constituents of serum and of tissues in hosts with certain malignancies and of tumors themselves. At this conference we have had methods described that I believe will yield pertinent information on the antigens of tumors, even if it turns out that their chief antigenic difference is a deficiency in so-called normal antigens. Such studies may also yield—and this may be equally important—a great deal of information on the antigens of normal cells.

Turning to the possibility of antiserums for diagnosis and treatment, it is apparent from this conference that various autoimmune, isoimmune, and heteroimmune phenomena should be studied. The problems of sensitized lymphocytes and of cell-bound antibody associated with delayed hypersensitivity also seem to be particularly promising.

In the event that no effective antiserums are found for the treatment of cancer, I am struck with the possibilities of nonspecific mechanisms that are being reported. Certainly we should explore further the use of organ-specific antibodies to localize radioactive isotopes or other antitumor substances at the site of tumors, even though these antibodies may not act directly on the tumors.

I think a remarkable possibility is suggested by the studies of Rapport and Graf: that a comparatively simple carbohydrate-lipide antigen may be synthesized that may stimulate the formation of an antiserum specific for some antigen at a vulnerable site in the tumor cell.

The several ways, noted by Mayer, in which red cells may be prepared for lysis by complement without using antiserums specific for the cell suggest interesting possibilities. Thus, certain nonred-cell antigens can be adsorbed on the red cell, and the resulting complex can be sensitized by specific antiserums to the nonred-cell antigens. Or non-immunologic reagents, such as tannic acid, can “sensitize” the red cell so that complement will lyse it.

In the field of measuring antibodies, Townes and his associates, cited by Osler, have carried out some particularly significant work. They used quantitative complement fixation to make reproducible estimates of lupus antibody, although the antigen has not been completely identified. This result depends basically upon the formation of complexes between nucleoprotein preparations and γ-globulins from the serum of patients with systemic lupus erythematosus that elicit the L. E. cell phenomenon.

From the standpoint of immunology, the evi-
dence that autochthonous tumors may regress or that potentially malignant cells may lie dormant for long periods, even though they do not completely disappear, may be of basic importance. There seem to be certain parallelisms between such tumors and some of the slowly developing infections produced by animal parasites (4). For the most part, these parasites are not toxigenic and, in laboratory slang, are "poorly antigenic." They produce long, chronic, or relapsing infections. These the zoologist terms "successful parasitism," but they are often associated with the production of antibodies that suppress the metabolism of the parasite without, in many cases, producing any lethal effect except after long-continued action.

To me, the most interesting of these is ablastin, the antibody produced in the rat against *Trypanosoma lewisi*. This antibody, which I described in 1924 (3), suppresses division of the nucleus and other organelles of the trypanosome. Once it is formed and the trypanosomes are unable to reproduce, the inhibited parasites survive for varying periods but are eventually eliminated by trypanocidal antibodies or by gradual phagocytosis.

The first study on the metabolic effects of ablastin was made by Moulder (2). He showed that, as the antibody developed in the rat, the carbohydrate metabolism of the trypanosomes changed from one of oxidative assimilation to one of maintenance.

More recently, Pizzi and I (6) reported that passively transferred antibody in 2 days suppresses the parasite's nucleic acid synthesis by as much as 87 per cent and suppresses its protein synthesis by 66 per cent. As ablastin is formed during ordinary infections, nucleic acid synthesis is completely inhibited in about 10 days, and protein synthesis is also markedly inhibited by this time but continues for several weeks at a low and continuously decreasing rate.

It is also interesting that Pavlinova and I (5) found a natural ablastic factor, as well as an acquired ablastin in mice infected with the closely related species, *Trypanosoma duttoni*. The natural factor was lost after splenectomy but could not be associated with any passively transferable serum factor.

I am now studying the mechanism of ablastic action on *T. lewisi*. It may possibly be an antinucleic acid. Moulder's results may indicate that reproductive inhibition in the trypanosomes is associated with the carbohydrate side of nucleic acid synthesis.

Ablastin may be effective in other situations. Thus, Campbell (1) has described an antibody against larval tapeworm infections that acts slowly and kills the cysticerci only after full development has taken place.

It is conceivable that a search for similar specific mechanisms in tumors might yield valuable information.

REFERENCES

Whither Bound—How and Why?

William H. Taliaferro