multiplication of untransformed cells, has proved and still proves to be enormously useful but tumour virologists are increasingly exploiting additional biochemical parameters.

Rubin and his colleagues, for example, have recently established that chick cells transformed by Rous sarcoma virus take up glucose and 2-deoxyglucose from their medium at a faster rate than untransformed cells although the rate of uptake of these sugars also depends on a cell's physiological state and in particular the rate at which it is dividing. This second observation raised doubts as to the relationship between enhanced uptake of sugars and transformation *per se*, but now Martin, Venuta, Weber and Rubin (*Proc. US Nat. Acad. Sci.*, **68**, 2739; 1971) have, by exploiting the temperature sensitive mutant T5 of Rous sarcoma virus isolated by Martin (*Nature*, **227**, 1021; 1970), shown that the increased rate of uptake of 2-deoxyglucose by transformed cells indeed depends on the expression of the transforming Rous sarcoma genome.

They report that when chick cells transformed by Rous virus and untransformed cells are growing at the same rate the transformed cells take up 2-deoxyglucose at a rate which is three times faster than the untransformed cells. Cells transformed by the mutant T5 and cultured at the permissive temperature of 36° C behave like cells transformed by wild type virus. But when mutant transformants are shifted to the nonpermissive temperature, 42° C, the rate at which they take up this sugar falls, without any detectable lag, such that by 12–24 hours after the shift the rate is that of untransformed cells. And when the transformants are returned to 36° C their rate of uptake once more increases. In short, transformed cells growing in the same conditions as untransformed cells exhibit a faster rate of uptake of 2-deoxyglucose and this difference depends, however indirectly, on the continued expression of the transforming Rous sarcoma genome. Furthermore, as experiments with cytosine arabinoside prove, the enhanced uptake of sugars by transformed cells is not dependent on DNA synthesis.

The mechanism which regulates the rate at which sugars are taken up by cells may well involve changes in the chemistry of the cell surface, a most fashionable subject for investigation among tumour virologists these days. Sachs and his colleagues, for example, report in the same issue of the *Proceedings* (*ibid.*, 2748) their latest experiments with concanavalin A and other lectins. They claim that SV40 transformed cells cultured at 24° C are much more readily agglutinated by concanavalin A than untransformed cells but at 4° C this difference between transformed and untransformed cells cannot be detected; neither are agglutinated. At both 24° C and 4° C, however, both transformed and untransformed cells bind the same amounts of concanavalin A. Furthermore, after exposure to trypsin at 24° C untransformed cells are agglutinated by low concentrations of concanavalin A but after exposure to trypsin at 4° C neither transformed nor untransformed cells are agglutinated by low concentrations of this lectin.

From these data Inbar, Ben Bassat and Sachs argue that the sites which bind concanavalin A are not affected by temperature changes but the component of these sites which determines agglutination is temperature sensitive and transformation sensitive. The agglutination sites may well be associated therefore with some specific metabolic activity. Inbar *et al.* comment that this conclusion does not hold for two other lectin binding sites, those for wheat germ agglutinin and soybean agglutinin, which are not apparently temperature sensitive. And what is perhaps even more intriguing, Sachs and his colleagues remark that there is a correlation between the activity of the component of the concanavalin sites that is involved in agglutination and the malignancy of a cell; but that is to be another story.

T Cell Activation by Histocompatibility Antigens

THE general concept that lymphocytes of the mouse can profitably be classified as either T or B cells is now widely accepted. T cells are easily defined as those lymphocytes which have undergone differentiation in the thymus; their precursors moved to the thymus from either the bone marrow in an adult or an equivalent haematopoietic organ, probably the liver, in the foetus. The definition of B cells is less easy because it is by no means certain whether the mature B cell arises in the bone marrow or from a precursor cell which must leave the marrow to undergo proliferation and specific differentiation elsewhere. Functionally, however, the B cell seems, unlike the T cell, to have the capacity to differentiate into an antibody secreting cell and thus in spite of its slightly murky origins it can usefully be delineated as a cell species.

The functional characteristics of T cells are still a matter of some dispute and the arguments concerning them touch on the fundamental question of whether the immune process is instructive or selective. Most immunologists favour some form of selective mechanism, whereby an immune response proceeds because of selection from a heterogeneous cell population of those cells best equipped to deal with a particular antigen. The nature of the heterogeneity in this last instance is one of the central problems of immunology. Sprent and Miller, in an article in next Wednesday's *Nature New Biology*, study these problems and reveal how the careless adoption of a word can lead to unorthodoxy.

The Australian school of lymphocyte function has contributed much to the literature in recent years. Among their efforts has been the demonstration that when thymocytes along with an antigen, often heterologous erythrocytes, are injected into mice which have been lethally irradiated, the injected cells react to the antigen by blast cell transformation; when transferred, along with more antigen, from the primary host spleen into a secondary irradiated animal the reacting cells display a specific capacity to cooperate in the ensuing immune response. The procedure at one time was referred to as "education". The full semantic horror of this nomenclature has now been realized, and Sprent and Miller offer "activation" as the preferred alternative.

Sprent and Miller describe the injection of parental strain thymocytes or thoracic duct lymphocytes into lethally irradiated F_1 hybrid mice. The injected cells proliferate in response to the antigens, foreign to them, of the other component of the hybrid and, after a period of intensive activity in the spleen and mesenteric lymph nodes, blast cells appear in the thoracic duct lymph.

These primed cells, when transferred to a second similar hybrid recipient, are capable of responding more quickly than a comparable unprimed thoracic duct lymphocyte population and, more interestingly, are much less capable of responding to a third party antigen—in an appropriate hybrid recipient—than are unprimed cells. The process of activation thus either involves selection of a specifically reactive cell population or it involves rapid restriction of an initially wider reaction potential.

It is interesting that activated parental cells collected from the thoracic duct of F_1 irradiated mice did not induce a splenomegaly reaction when injected into appropriate newborn F_1 recipients, and it was impossible to demonstrate the activated state beyond second transfer into irradiated F_1 recipients. This finding, which suggests a restriction on the proliferative capacity of T cells in response to continued antigenic stimulus; contrasts with the suggestion (Askonas *et al.*, *Proc. US Nat. Acad. Sci.*, **67**, 1398; 1970) that B cell populations have a capacity for repeated response to antigenic stimulus during a series of transfers in irradiated host mice.