invitations and other mailings of interest are sent to them periodically. Services are available for the wives and families of these foreign physicians. We have also instituted an annual series of symposia[3] for directors of medical education, hospital directors, chiefs of services and others responsible for foreign house staff. These symposia cover various aspects of the problems involved with foreign medical graduates, and attempt to provide a forum for the exchange of ideas and information among those who come in closest contact with them.

The Philadelphia program has developed from close cooperation between the medical community and lay organizations interested in service to foreign visitors. We hope it will become a prototype for the development of similar programs in other parts of the country.

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IMMUNOSUPPRESSION AND MALIGNANT NEOPLASMS

To the Editor: Simmons and his associates (New Eng J Med 283:190-191, 1970) have taken a position against the discontinuance or lightening of immunosuppressive therapy in organ-homograft recipients in whom de novo cancers have developed. Their argument is based almost entirely on observations of a patient who actually *did* stop steroid therapy toward the end of her life, who then displayed evidence of recovered immunological reactivity by promptly rejecting her renal homograft, which had hitherto been functioning for four years, and who died 16 months after the diagnosis of disseminated dysgerminoma had been made. At autopsy, residual tumor could not be found. Leaving aside the question of how effectively the patient had reduced her own immunosuppression, the term "cure" of a cancer as it appears in the title should be questioned even in an immunologically competent person after so short a follow-up period.

Since the first description of de novo malignant neoplasms in renal-homograft recipients in 1968[1,2] there have been 40 known cases of this complication, of which 11 have been in our institutions. The 14 patients with superficially located epithelial neoplasms (skin, lip and uterine cervix) were *all* effectively treated by standard surgical technics without risking the homografts by reductions in immunosuppression. Even in such cases, the neoplasms may present special problems since one of our kidney recipients, 41 years of age, has already had three squamous-cell carcinomas of the skin removed in his 7½ years of post-transplantation life.

The epithelial tumors within the abdomen and chest and the mesenchymal cancers in all locations have not been controlled with this approach: eight of nine "deep" carcinomas and 16 of 17 mesenchymal tumors have led or contributed to early death. The exceptional patient in the deep epithelial group was the one described by Simmons et al., and since she died, it cannot be established for certain what the natural behavior of the dysgerminoma might have been. The surviving patient in the mesenchymal group was treated at our center by radiotherapy of her brainstem lymphoma 2½ years ago, in addition to a drastic reduction in immunosuppression. Details of all 40 patients from throughout the world in whom malignant neoplasms have developed in the post-transplantation period are being published[3,4] and will be provided upon request.

It may be that the contentions of Simmons et al. will ultimately prove to be correct. However, it is worth noting that the present evidence from our international compilation does not support their position, and that their arguments are based upon a case that so far is not only nonrepresentative but uniquely so. Consequently, it seems reasonable not to dismiss so readily as they have done the possibility of lightening immunosuppression in patients with post-transplantation carcinomas and lymphomas.

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2. Penn I, Hammond W, Brettschneider L, et al: Malignant lymphomas in transplantation patients. Transplantation Proc 1:106, 1969
3. Starzl TE, Porter KA, Halgrimson CG, et al: Long term survival after renal transplantation in humans: with special reference to histocompatibility matching, thymectomy, homograft glomerulonephritis, heterologous ALG, and recipient malignancy. Ann Surg 172: September, 1970
4. Penn I, Halgrimson CG, Starzl TE: *De novo* malignant tumors in organ transplant recipients. Transplantation Proc (in press)

The above letter was referred to the authors of the article in question, two of whom offer the following reply:

To the Editor: For a number of reasons, we consider it unlikely that transplanted patients in whom de novo malignant neoplasms develop will reject their tumors if immunosuppression is stopped. In the first place, although all experimental tumors induced by viruses or chemical carcinogens have tumor antigens, such antigens have been difficult to detect on tumors that are "spontaneous."[1] Secondly, even when such antigens have been found, they are poor immunogens as compared with the histocompatibility antigens normally responsible for allograft rejection. Thirdly, the vigor of rejection is directly proportional to the strength of the immunogenic stimulus. And, finally, tumors with weak antigens, even when known to be immunogenic, may be self enhancing – that is, antibodies are elicited that do not lead to the rejection of the tumor but to its further growth.[2] For these reasons, tumors that are transplanted inadvertently from the donor to the recipient possess the strong histocompatibility antigens of the donor and will be rejected upon cessation of the immunosuppression.[3] Spontaneous tumors with weak or absent immunogens that are well enhanced are not likely to be rejected when immunosuppression is stopped. Certainly, the kidney will be rejected first. Thus, to hope that a drastic reduction in immunosuppression will allow the patient to reject the tumor without rejecting the kidney is probably futile. The patient with a tumor but without a good, functioning kidney is certainly at a great disadvantage.

Thus, we believe strategy for this rare complication is conventional therapy directed toward obliterating the tumor without altering the existing immunologic balance. The patient discussed had manifested four severe renal rejection episodes during her post-transplant course. Thus, when she stopped taking prednisone for one month (but maintained herself on azathioprine), the kidney was rejected. It is unlikely that the brief period of partial immunological rebound led to the *complete* obliteration of *all* traces of the tumor. The Denver patient, on the other hand, did not *even* reject

her kidney when immunosuppression was stopped, and it is likely that her remission was due to the radiotherapy alone.

We agree with the following points of the Denver group: the patient may not have been "cured," but no remnant of tumor was present at death; epithelial neoplasms can be treated by standard therapy without endangering the allograft; and we must reserve judgment in the treatment of "deep" tumors. The tentative nature of our conclusions is reflected in the concluding paragraph, in which the words "possible", "one would not expect" and "probably" are used.

Starzl and his co-workers have made the greatest contribution to this field. We apologize for inadvertently omitting reference to their published paper (reference 2 in the above letter).

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MELANOMA-SPECIFIC ANTIGENS

To the Editor: The recent article of Jehn et al. on melanoma-specific antigens (New Eng J Med 283:329-333, 1970) was both very interesting and disturbing to me. First of all, the number of patients apparently sensitized to the tumor extracts is exceedingly high (seven of seven). I should therefore like to know if the authors chose to present only reacting patients and, if so, the total number of patients with melanoma studied.

Secondly, as a control to exclude definitely tumor-unrelated reactions, I believe that similar extracts from normal skin tissue or benign pigmented lesions should have been tested as possible mitogenic agents. Were these experiments done, and what were their results?

Finally, a brief comment on the relevance of intracellular versus membrane-located tumor-specific antigens to the host's immune response in vivo would be appreciated.

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The above letter was referred to the authors of the article in question, two of whom offer the following reply:

To the Editor: To answer Dr. Piessens's questions in order, in the first place, there was no selection: seven consecutive patients were studied. All patients had metastatic disease and the extent of their disease varied from regional-lymph-node involvement to distant visceral metastases. Judging from the results of ^{3}H-thymidine uptake by their lymphocytes, not all patients were sensitized to the same degree.

Secondly, we did not measure lymphocyte transformation in the presence of tissue extracts from a benign pigmented lesion.

Finally, we did not study intracellular and membrane antigens. This has been done by Lewis et al. (Brit Med J 3:547, 1969). It seems to us that membrane antigens might be more important than intracellular antigens in the postulated immunologic defense mechanisms against malignant cells.

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CORRELATION OF THYROID-FUNCTION STUDIES

To the Editor: The last 10 years have seen the development of several new tests of thyroid function. This proliferation of examinations has confronted the physician with the difficult decision of selecting the test that will give him the most meaningful and accurate data.

It is generally recognized that in the absence of contamination with iodine or other drugs, the uptake of ^{131}I by the thyroid gland has a diagnostic accuracy of 83 per cent for hyperthyroid and 73 per cent for hypothyroid patients. The measurement of serum thyroxine by competitive protein binding has an accuracy of 90 per cent in both conditions.[1]

The uptake of ^{131}I is a measure of the iodine-trapping ability of the gland, whereas the determination of serum thyroxine by competitive protein binding is a measure of circulating thyroid hormone.[2,3] In spite of measurements of different aspects of thyroid function, there appears to be a high degree of correlation between these two examinations. In an attempt to demonstrate this relation, 140 patients were studied, of whom six were hypothyroid, 29 euthyroid, and 105 hyperthyroid.

Of these patients the average serum thyroxine level was 22.16 μg per 100 ml in the hyperthyroid group, 8.67 μg per 100 ml in the euthyroid group and 2.3 μg per 100 ml in the hypothyroid group.

The ^{131}I uptake among the hyperthyroid patients averaged 57 per cent; in the euthyroid group the value was 25 per cent, and the hypothyroid patients had an uptake average of 6 per cent.

The correlation coefficient for the hypothyroid group was 0.91, whereas for the hyperthyroid patients, the value was 0.86 and for the euthyroid patients, the coefficient was 0.88. The correlation coefficient for the entire series of 140 patients was 0.88.

By using these two tests in evaluating the patient with suspected thyroid disease, the clinician can feel confident that he is using the examinations that not only yield the highest degree of accuracy but also reflect a significant degree of correlation.

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2. Ingbar SH, Woeber KA: The thyroid gland. Textbook of Endocrinology. Edited by RH Williams. Philadelphia, WB Saunders Company, 1968, pp 142-162
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VITAMIN PREPARATIONS FOR PATIENTS WITH PARKINSONISM

To the Editor: Parkinsonism and pernicious anemia are both diseases of late adult life. The exact prevalence of these diseases is unknown, but a reasonable estimate would be approximately 100 per 100,000.[1,2] Doses of vitamin B_{12} of