investigation of strength of materials. There has been, however, a great need for a book describing in simple language the elements of photoelastic measurements, and this gap seems to be filled by Filon's "A Manual of Photoelasticity for Engineers." It gives first a short introduction of the physical fundamentals of photoelastic methods, and then applies this knowledge to the treatment of instruments and measurements.

The great productivity in the field of general physics texts and of many specialized advanced texts is of course stimulated by the interest in modern physics and physical research in this country. Still there exists a great gap which has not yet been filled between the introductory text and the specialized treatise. Any physicist who has occasion to discuss physical problems with chemists, biologists or engineers is often confronted with the following plea: The Germans have Kohlrausch's "Practical Physics" or Riecke's two-volume text on physics; physico-chemists, in this country, have the excellent work of Hugh C. Taylor and his collaborators; physiologists can refer to Bayliss's standard text, but there is no physics text, in the English language, of this character, a book that makes it possible for scientists working in other fields to obtain an adequate knowledge in physics beyond the elementary text and without going to specialized handbooks. May we express the hope that the American Physical Society and the Association of American Physics Teachers will soon find means to prepare a text-book in physics to meet this demand!

K. LARK-HOROVITZ

PURDUE UNIVERSITY

SPECIAL ARTICLES

HETEROLOGOUS TRANSPLANTATION OF HUMAN AND OTHER MAMMALIAN TUMORS

VARIOUS claims to the successful grafting of human cancers to lower species of animals have not been substantiated by repetition, and at the present time the view generally held by workers in the field of cancer research is that such transplantation is impossible. In fact, the heterologous transplantation of tumors between even closely related species has met with little success. Murphy[1] was able to grow the Jensen rat sarcoma in developing chick embryos, and the successful transplantation of mouse carcinomata to rats has been independently reported by Shirai,[2] Putnocky[3] and others.

The transplantation of a uterine carcinoma of the rabbit into the anterior chamber of the eyes of other rabbits has been reported.[4] The ease with which the initial transplantation was made, in contrast to the complete failure of other modes of inoculation, suggested that this method might be used successfully for heterologous transplantation. The success of early attempts was recorded in the paper just mentioned. However, in view of the obvious importance of heterologous transplantation to both biology and cancer research, a preliminary report of the successful growth of rabbit tumors in other species of animals through serial generations and of a human cancer in rabbits seemed desirable.

Two rabbit tumors, an adenocarcinoma of the uterus and an adenocarcinoma of the breast have been successfully transplanted into the eye of the guinea pig. The methods employed were described in detail in the paper referred to above.[4] Transplantations were always made under anesthesia. The uterine tumor was taken from the sixth rabbit generation and so far has been transplanted serially through three generations in the guinea pig. The breast tumor was transferred to the guinea pig after two generations in the rabbit and is now growing in the second guinea pig generation.

Growth of the tumor in the foreign species presented the same characteristics as in the natural host. Microscopic examination of heterologous transplants show that so far the histological character of the tumors has remained unchanged. The cells of the transplant are descendants of the original neoplasm and not derivatives of the guinea pig.

The ultimate fate of the heteroplastic tumors is uncertain. At the present time, progressive growth has been observed in guinea pigs bearing the breast tumor for more than one hundred days and in pigs with transplants from the uterine tumor for as long as three months. So far, the tumors have not metastasized, but in no instance have the pigs been held for a period of time as long as that required for the development of metastases from homologous transplants.

A successful transplantation of a human scirrhus cancer of the breast has also been made, and slow but progressive growth has continued for more than eighty days.[5] In this instance, the transplantations were made during the summer months at a time when only a small percentage of homologous grafts are successful and growth rates are much reduced. Moreover, two hours

[1] J. B. Murphy, *Jour. Exper. Med.*, 17: 482, 1913.
[2] Y. Shirai, *Japan. Med. World*, 1: 14, 1921.
[3] J. Putnocky, *Ztschr. für Krebsforsch.*, 32: 520, 1930.
[4] H. S. N. Greene and J. A. Saxton, Jr., *Jour. Exper. Med.*, 67: 691, 1938.

[5] This tumor was obtained through the kindness of Dr. R. A. Moore and Dr. W. A. Cooper, of the Cornell University Medical College.

elapsed between biopsy and transplantation of the tissue.

Despite these conditions, the human tumor has grown in seven of the twelve rabbits used. Growth first became apparent toward the end of the third week when the rough edges of the fragments became rounded and their color changed to a pinkish-yellow in contrast to the dull white of pieces that failed to grow. The extension of blood vessels from the iris into the transplant occurred in four of the animals between the thirty-fifth and fortieth days. Vascularization has not occurred to date in three of the animals in which primary growth was observed, but notwithstanding the fragments have continued to increase in size.

The growth rate increased following vascularization, and at the present time the transplants are approximately five times their original size. In two instances the pieces are attached to the cornea, which has apparently been invaded by tumor cells and extension to the outside is imminent. In the remaining instances, the transplants are attached to the iris, and irregular projections of growth may be observed in many planes.

In so far as heterologous transplantation from rabbit to guinea pig is concerned, it has been definitely established that the anterior chamber of the eye affords a means of transplantation of the tissues of one species into the body of another where apparently they may be continued indefinitely. The human cancer has not been carried as far, but since the behavior of the grafts conforms in all respects with those of rabbit tumors in guinea pigs, it seems highly probable that human tissues can also be maintained indefinitely in the foreign host.

The serial transplantation and growth of the tissues of a mature animal of one species in an animal of another species opens up a number of interesting problems. Among them is the question of the specific nature of the tissue ultimately grown in the foreign host. This and other problems are under investigation. Detailed results of this series of experiments will be reported elsewhere.

HARRY S. N. GREENE

THE ROCKEFELLER INSTITUTE
FOR MEDICAL RESEARCH,
PRINCETON, N. J.

REDUCED BLOOD COAGULATION TIME BY INJECTION OF STEROL EXTRACT OF LIVER

DURING a study of sterols extracted from the liver, a more rapid clotting of the blood was noticed after one of the lipid fractions was injected subcutaneously into a hypophysectomized-depancreatized dog. A preliminary investigation therefore has been made of the effect of this fraction in reducing the clotting time in animals with a hemorrhagic tendency from ligation of the bile duct and from a vitamin K deficiency. Dam[1] and Almquist and Stockstad[2] have described the production of a generalized hemorrhagic tendency in chicks fed a diet deficient in vitamin K and were able to prevent the bleeding tendency by the feeding or injection of extracts derived from alfalfa, hog liver fat, green vegetables and other sources. The reduced prothrombin of rats after bile duct ligation has been elevated by feeding vitamin K, in large amounts or with the addition of bile.[3] Highly potent concentrates of vitamin K which can be injected parenterally have been obtained by Almquist[4] and by Dam and Glavind.[5] They describe the vitamin as a non-sterol, unsaponifiable lipid. Osterberg[6] also described it as a non-sterol, which was alkali-labile and fairly heat-stable.

The substance we employed in this study is a sterol which is fairly stable to alkali and heat. It has been obtained from the livers of dog, lamb and pig by the following method of extraction. One kilogram of ground liver from a freshly slaughtered animal was extracted at 50° C. with 2 liters of 95 per cent. alcohol, which was acidified with 0.3 cc of concentrated HCl, and then re-extracted with 2 liters of 95 per cent. alcohol. The combined filtrates were saponified for 18 hours at 45° C with 50 grams of $Ba(OH)_2$ and 80 grams of NaOH, then held at 0° C for 4 hours before filtering at room temperature. After concentrating the clear dark amber solution to $\frac{1}{2}$ volume with reduced pressure at 40° C it was vigorously shaken with 500 cc of petroleum ether, the alcohol phase was diluted with an equal volume of water and shaken again. Two additional extractions were made with 200 cc portions of petroleum ether. Evaporation of the ether from the combined extracts left about 700 mg of a yellow crystalline material, soluble in about 10 cc of sesame oil at 38° C. Small amounts of this impure material gave a positive Salkowski and Lieberman Burchard reaction but negative Rosenheim and Pettenkoffer tests. Only a few milligrams of precipitate could be obtained by digitonin treatment of 500 mgm of the crude material.

The sterol fractions have been taken up in sesame oil for subcutaneous injection into normal and jaundiced rats and into vitamin K deficient chicks. Dogs have been used for the intravenous injections of the extract, suspended in an emulsion with lecithin in normal saline. For the determination of clotting time blood was drawn in the rat by syringe from the heart

[1] H. Dam, *Nature*, 133: 909, 1934.
[2] H. J. Almquist and E. L. R. Stockstad, *Jour. Biol. Chem.*, 111: 105, 1935.
[3] J. D. Greaves and C. L. A. Schmidt, *Proc. Soc. Exp. Biol. and Med.*, 37: 43, 1937.
[4] H. J. Almquist, *Jour. Biol. Chem.*, 120: 635, 1937.
[5] H. Dam and J. Glavind, *The Lancet*, 1: 707, March 26, 1937; H. Dam, J. Glavind, L. Lewis and E. Tage-Hansen, *Skand. Arch. Physiol.*, 79: 121, 1938.
[6] A. E. Osterberg, *Proc. Staff Meet., Mayo Clinic*, 13: 72, 1938.