20. Starzl, T. E., Groth, C. G., Brettschneider, L., Moon, J. B., Fulginiti, V. A., Cotton, E. K. and Porter, K. A.: Extended survival in 3 cases of Orthotopic Homotransplantation of the Human Liver. Surgery, **63**:549, 1968.
21. Starzl, T. E., Marchioro, T. L., Porter, K. A., Taylor, P. D., Faris, T. D., Herrmann, T. J., Hlad, C. J. and Waddell, W. R.: Factors Determining Short- and Long-Term Survival after Orthotopic Liver Homotransplantation in the Dog. Surgery, **58**:131, 1965.
22. Starzl, T. E., Marchioro, T. L., von Kaulla, K., Hermann, G., Brittain, R. S. and Waddell, W. R.: Homotransplantation of the Liver in Humans. Surg. Gynec. Obstet., **117**:659, 1963.
23. Starzl, T. E., Marchioro, T. L., Rowlands, D. T., Jr., Kirkpatrick, C. H., Wilson, W. E. C., Rifkind, D. and Waddell, W. R.: Immunosuppression after Experimental and Clinical Homotransplantation of the Liver. Ann. Surg., **160**:411, 1964.
24. Starzl, T. E., Marchioro, T. L., Porter, K. A., Iwasaki, Y. and Cerilli, G. J.: The Use of Heterologous Antilymphoid Agents in Canine Renal and Liver Homotransplantation, and in Human Renal Homotransplantation. Surg. Gynec. Obstet., **124**:301, 1967.
25. Stuart, F. P., Torres, E., Hester, W. J., Dammin, G. J. and Moore, F. D.: Orthotopic Autotransplantation and Allotransplantation of the Liver: Functional and Structural Patterns in the Dog. Ann. Surg., **165**:325, 1967.
26. Terasaki, P. I., Vredevoe, D. L. and Mickey, M. R.: Serotyping for Homotransplantation. X. Survival of 196 Grafted Kidneys Subsequent to Typing. Transplantation, **5**:1057, 1967.
27. von Kaulla, K. N., Kaye, H., von Kaulla, E., Marchioro, T. L. and Starzl, T. E.: Changes in Blood Coagulation Before and After Hepatectomy or Transplantation in Dogs and Man. Arch. Surg., **92**:71, 1966.

Discussion

Dr. Francis D. Moore (Boston): Dr. Starzl's work in this field is absolutely outstanding and for those of us interested in liver transplantation, this is a banner day when we can contemplate four patients alive and well with lethal liver disease removed and a new liver in place. This is a magnificent achievement and liver surgery as of this day has an entirely new look from hither forward. But I would like to use this opportunity to discuss another aspect of Dr. Starzl's work.

Four years ago, at the Society of University Surgeons, when Dr. Starzl's initial clinical experience and ours likewise had ended with fatality, it was clear (and so stated at the meeting) that more progress was needed before it would be ethically, morally, surgically and scientifically acceptable to move ahead again with clinical liver transplantation.

Immunosuppression without hepatotoxicity was essential, as well as improved perfusion-storage. Now these things have come to pass, especially by the development of anti-lymphocyte globulin, and it is appropriate again to move ahead. If this forward motion is undertaken by persons or departments that have practical capability in transplant immunology and histocompatibility matching, as well as surgical experience with transplantation and the postoperative care of patients on immunosuppression, there is no need for consultant boards to declare the patient operable or a team from another institution to decide that the donor is dead.

The time-temperature curves for liver donation, the permissible normothermic dead-time, and the prior state of death are the same for liver donation as for heart, with the heart somewhat less vulnerable to normothermic ischemia.

There has recently been a statement issued by a committee in Washington that attempts to deal with these matters as applied to the heart. As nearly as I can see, none of the authors of this document has busied himself with the transplant problem over these last 15 years; the document makes no reference whatsoever to the long work of many Departments in this country who have labored through the difficult years of transplantation, nor does it acknowledge the obvious fact that actual experience in immunogenetics, immunosuppression and surgical transplantation are the essential normal prerequisites to moving ahead with any newly transplantable organ.

Nor does it make reference to the fact that the moral security of the next 25 years of American surgery, in exploring this new field, will rest secure just where it has in the past 20 years: in giving free and untrammelled opportunity for development to those Departments and individuals that are willing to take the time and trouble to develop both the immunological and surgical aspects of organ transplantation, as Dr. Starzl has demonstrated today with a project that was held in abeyance until the fundamentally ethical nature of science itself indicated that it was time again to move ahead.

Dr. Eric W. Fonkalsrud (Los Angeles): I would like to congratulate Dr. Starzl and his associates for their very excellent contributions to furthering the knowledge of both liver preservation and transplantation, and for their remarkably good clinical results, shown in this study.

We have followed Dr. Starzl's work with very great interest, however have used a slightly different technic in the laboratory and in one patient.

The emphasis in our studies has been on the use of hepatic cell stabilizing drugs, such as chlorpromazine and cortisone administered to the donor after death followed by external hypthermia to the graft after excision. A siliconized internal vascular shunt has been used to decompress the inferior vena cava and portal vein to the right atrium in the recipient.

This slide [slide] shows the liver of a 2½-year-old boy with biliary atresis who underwent orthotopic liver transplantation. The total time of liver ischemia was 91 minutes.

This photograph shows how pink and uncongested the graft appeared 30 minutes after revascularization. The falciform ligament and suspensory ligaments of the grate were attached to the diaphragm in this patient, not so much to prevent arterial kinking as to provide support to the vena caval anastomosis.

The patient recovered from the operation rapidly and experienced a drop in bilirubin from 33 to 4.5 mg./100 ml. and alkaline phosphatase from 115 to 15 KA units within 24 hours. There was prompt good bile excretion which was drained externally. Immunosuppression was started on the day of operation and continued as in Dr. Starzl's study.

The patient was ambulatory and taking a regular diet when, on the fourteenth day, he promptly became septic—and developed air under the right diaphragm as is shown on this abdominal roentgenogram. Exploration showed a large area of necrosis in the dome of the right lobe of the liver, as is shown on this slide. Postmortem showed thrombosis of the small branches of the right hepatic artery, as is seen in this photograph, and which is very similar to those described in Dr. Starzl's paper today. All of the major vascular anastomoses were patent.

This photomicrograph shows an area of relatively normal liver tissue with ductal proliferation in the area that was not infarcted. The area of transition between the infarct and the normal liver tissue is clearly seen. I would like to ask Dr. Starzl if he has an explanation for why arterial thrombosis occurs so late after grafting and if he believes there may be additional causative factors such as a manifestation of rejection? Do you believe that adding arterial blood to the portal vein may be of any benefit in these patients? Would short- or long-term anticoagulation be of any help?

DR. THOMAS E. STARZL (Closing): I would like to thank Dr. Moore not only for the thoughts he expressed, but for the kindness he has displayed to us this afternoon and at all times in the past, which has made it possible for our two institutions to exchange data long before it was published.

The approach to preservation described by Dr. Fonkalsrud is a different one than we used in our cases. We were anxious to obtain longer term preservation than we have ever found possible with such simple perfusion methods. With our recently used technic we have been able to see the liver within the chamber and to evaluate it under circumstances of perfusion before anything was done to the recipient.

As to the cause for the late thrombosis, I think one can only speculate. It seems likely to us that the mechanical defect which I demonstrated earlier may not be completely occlusive and that there may be added factors, as Dr. Fonkalsrud suggested. Possibilities might include the swelling that occurs in liver homografts at the time of active rejection, or alternatively the diminished blood flow that is very often seen in the canine liver at the time of a potentially reversible rejection. With a combination of any of these circumstances, infant livers with their fragile arteries might be subject to a special risk of dearterialization.