References and Notes

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Instrumentation of Fetal Electrocardiography

During the past two decades maternal mortality has been progressively reduced. With the same standard of pediatric care, the reduction in stillbirths and neonatal mortality has been only a small fraction of the gain made in maternal mortality. In addition to the 160,000 infant deaths associated with the birth process each year, there are a large number of infants afflicted with cerebral palsy and mental retardation. It is possible that these problems find a common basis in fetal anoxia.

If significant gains are to be made in this area, a reliable means of accurately determining reversible "fetal distress" must be found. The present "normal" parameters of the fetal heart rate during labor have been charted from periodic auscultatory sampling and are therefore open to some question. If "fetal distress" is to be defined in terms of fetal cardiac rate and rhythm, the limits of "normal" must be defined accurately.

Because only minute amounts of fetal energy are available for study on the anterior abdominal wall of the mother, the basic problem is one of instrumentation. The types of fetal energy which can be detected with present instrumentation are as follows: (i) electric energy—electrocardiogram and electroencephalogram—and (ii) mechanical—phonocardiogram and infrasonic (less than 15 cy/sec).

Since Cremer's (*1*) success in recording the fetal electrocardiogram in 1906, there have been a number of reports of fetal electrocardiographic studies. By and large, the instrumentation has been limited to some type of preamplifying apparatus used with a standard electrocardiographic machine or an electroencephalograph. In many instances fetal *QRS* complexes were identified, but there are few records that show consistently recognizable *P* and *T* waves.

This preliminary report (*2*) outlines an instrumental approach to fetal distress using fetal electrocardiography for determination of the normal fetal heart rate throughout the course of labor and the notation of any changes of rate and rhythm which may be related to uterine

contractions or abnormal obstetrical conditions.

In order to record accurately the fetal heart rate throughout labor, some means of removing the maternal electrocardiogram must be employed, since both electrocardiograms are present as vectors in a volume conductor. In principle, this is done by in-phase canceling of the maternal complex in a differential amplifier (Fig. 1). One input channel is connected to electrodes from the lower abdomen of the pregnant patient, where both maternal and fetal electrocardiograms are present. The other input channel is connected to two electrodes on the upper abdomen, where the maternal electrocardiogram alone is present. This maternal complex should be of the same configuration and amplitude as the lower one, for it is used for cancellation. Discrimination against outside electric interference is achieved by using differential amplifiers ahead of the canceling amplifier.

The tracings shown in Fig. 2 demonstrate experimental results that can be duplicated in the majority of patients throughout the course of labor. However, the necessity for matching and balancing one complex against another is a disadvantage, and current exploration of a system for rectification, integration, differentiation, and gating appears to offer a simpler solution.

In order to provide the most accurate definition of the normal fetal heart rate during labor, it is desirable to record it continuously and relate it graphically to the amplitude of the uterine contractions. Experimentally, this is a laborious task. In a 10- to 15-hour labor there are about 100,000 to 150,000 pulse intervals to be measured and plotted against about 150 uterine contractions. Currently it takes about 150 hours of technician's time to process one complete labor. If any reasonable number of labors are to be studied, some type of semiautomatic data-reduction system must be used.
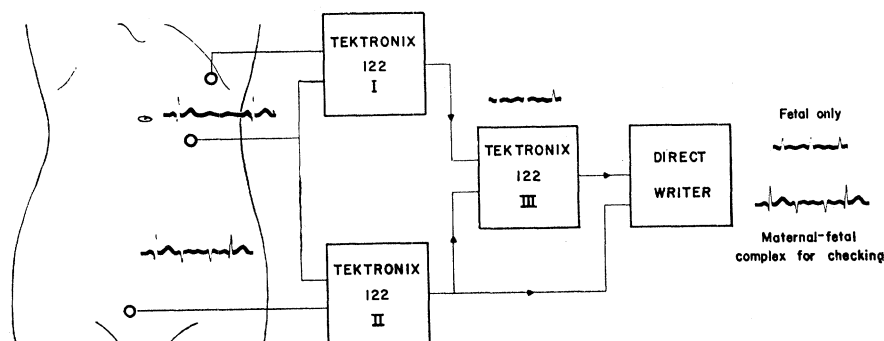

Fig. 1. Apparatus for cancellation of the maternal electrocardiogram. The Tektronix model 122 preamplifiers were connected as shown; the two-channel, direct-writing electrocardiograph is manufactured by the Elema Instrument Co., Stockholm, Sweden.
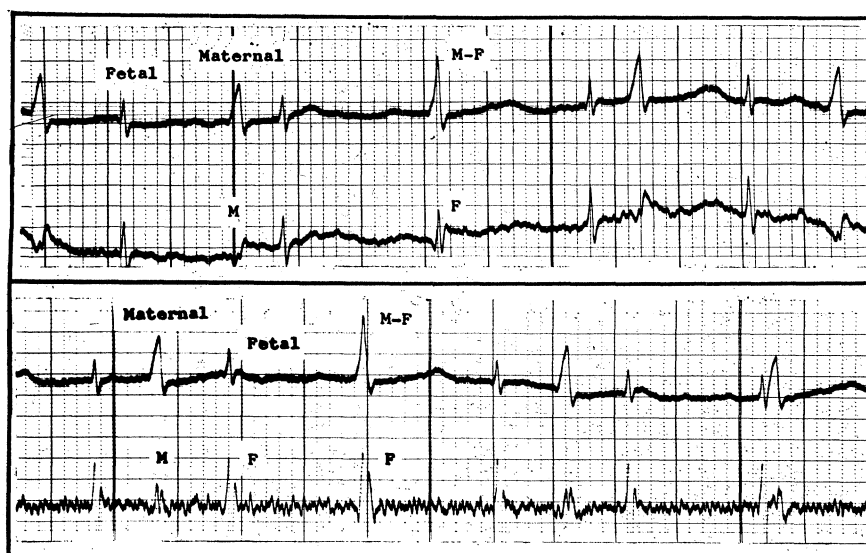

Fig. 2. Cancellation of maternal electrocardiogram: two records obtained with the two-channel electrocardiograph. The upper channels of both tracings show maternal and fetal electrocardiograms. The lower channels show only the fetal electrocardiogram, with cancellation of the maternal electrocardiogram. The lower channel of the bottom tracing shows differentiation for electronic counting.

A system is being developed to reduce the data. The raw data will be recovered from magnetic tapes, and a very compact record will be provided by a two-channel, direct-writing oscillograph if the fetal heart rate falls within predetermined "normal" limits. If these are exceeded, the time base of the writing system will be automatically increased, and a more detailed record will be secured. At the same time, the information will also be digitized and plotted by an $x - y$ recorder.

It is hoped that the use of modern instrumentation methods may aid in the elucidation of clinical fetal distress.

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2. This study is being supported by research grants from the Medical Fluid Research Fund of Yale University, the Association for the Aid of Crippled Children, and the National Heart Institute, National Institutes of Health, U.S. Public Health Service (grant No. H-2272). We are indebted to C. L. Buxton, professor and chairman of the department of obstetrics and gynecology, to W. Watson, chairman of the department of physics, and to Andrew Patterson, Jr., department of physical chemistry, for many helpful suggestions and guidance in this study. We wish to thank the Burdick Corp. of Milton, Wis., for providing us with the two-channel Elema electrocardiograph and Tektronix, Inc., Bronxville, N.Y. for their cooperation with the instrumental aspects of this study.
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Intraocular Arterial Homotransplants for Studying Atherosclerotic Lesion Regression

The purpose of this report (*1*) is to introduce the use of intraocular arterial homotransplantation for studying spontaneous or experimentally induced regression of specific atherosclerotic lesions in healthy animals. The operative procedures used were modifications of those employed by several investigators (*2*). A portion of an artery is excised aseptically and atraumatically from an anesthetized donor animal, rinsed with warm (37°C) mammalian Ringer's solution, and opened longitudinally with sharp scissors. Square pieces of approximately equal size are cut from selected normal or uniformly atherosclerosed areas. One piece is retained as a control for histologic study and for comparison with transplants removed later in the course of the experiments. The others are placed in warm Ringer's solution until they are transplanted into the host animals.

Each of the anesthetized host animals

is taped securely to an animal board to minimize reflex head movements during the operation. Three drops of 0.5-percent tetracaine hydrochloride solution are applied topically to the eye into which a transplant will be made. The sclera is grasped firmly with fixation forceps, and a 3- to 4-mm incision is made through the cornea, near the corneoscleral junction, with a cataract knife. While one edge of the cut cornea is gently lifted with sharp-pointed forceps, a corner of one of the transplants is grasped with slender mouse-toothed forceps and gently inserted through the incision into the anterior eye chamber. A slender blunt instrument (strabismus hook) is used to slide the transplant across the anterior eye chamber to the opposite side and wedge it there between the cornea and iris with the intimal surface facing outward. Finally, a small amount of penicillin ointment is applied to the operated eye. Depending on the experimental plan, transplants of either normal or atherosclerotic arteries may be made into one or both eyes of each host.

Several groups of animals may be prepared. For some experiments, healthy young litter-mate animals of the same sex should comprise an experimental group and serve as hosts for arterial transplants taken from a litter-mate of the same sex. For other experiments, animals of the same or opposite sex from another litter of the same species and strain could be used. In either case, the donor may or may not have been subjected to atherogenic procedures.

At selected times (for example, every 3 months), a host animal of each group can be sacrificed, and histologic sections of the normal and atherosclerotic transplants can be prepared by the same methods as those used for the control pieces. The sections of control and transplanted pieces from each group can then be studied to determine the nature and degree of any structural or chemical
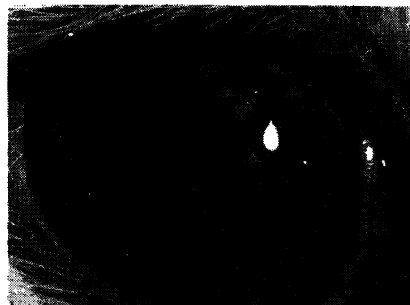

Fig. 1. Homotransplant of atherosclerotic aorta in the anterior eye chamber of a young female rabbit, 4 weeks postoperatively. Note the extensive invasion of the thickened intima by blood vessels from the iris.
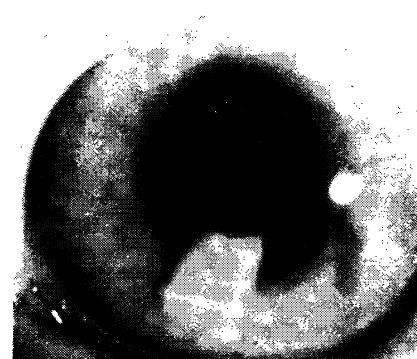

Fig. 2. Homotransplant of normal aorta in the anterior eye chamber of a young female rabbit, 4 weeks postoperatively. No blood vessels invading the intima can be observed.

changes, or both, which may have occurred in the transplants, either spontaneously or as the result of experimental procedures on the host. It may also be possible to determine the order in which each of several changes occurs. Comparison of the results obtained using dogs, rats, or other resistant species with those obtained from rabbits and other susceptible species may reveal some of the reasons for species differences in susceptibility to experimental atherosclerosis.

In experiments with rabbits, recovery of the host animals from the operation is prompt and is not complicated by infection. The adventitia of all the normal and atherosclerotic transplants becomes attached to the anterior surface of the host's iris by fibroconnective tissue in less than 8 days. Within 30 days, the adventitia of all the transplants is invaded by several clearly visible blood vessels from the iris. In addition, the thickened intima of all atherosclerotic transplants becomes extensively vascularized (Fig. 1), but that of the normal transplants does not (Fig. 2).

The transplants of normal aorta have been in place for 6 months, and those of atherosclerotic aorta for 6½ months. It has not been determined how much longer than this they will persist, but apparently there will be sufficient time to permit long-term studies of the effects of drugs, diets, and other experimental regimens on the structure and blood supply of the transplants. These test animals should be more responsive to drugs and diets that may cause regression of atheromata than animals which have been subjected to rigorous atherogenic procedures. Should certain procedures be found to accelerate regression of the transplanted lesions, their application to the treatment of human atherosclerosis is indicated.

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