

PHYSIOLOGY OF PREMATURITY

TRANSACTIONS OF THE FIRST CONFERENCE
MARCH 21, 22, AND 23, 1956

CONTENTS

Fetal-Maternal Endocrinology in Late Pregnancy
Fetal and Placental Circulation in Late Pregnancy

EDITOR

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THE JOSIAH MACY, JR. FOUNDATION

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Edited by
JONATHAN T. LANMAN, M.D.
DEPARTMENT OF PEDIATRICS
NEW YORK UNIVERSITY-BELLEVUE MEDICAL CENTER
NEW YORK, N. Y.

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TABLE OF CONTENTS

First Conference on Physiology of Prematurity

The Josiah Macy, Jr. Foundation Conference Program:

Frank Fremont-Smith 7

Introductory Remarks:

Clement A. Smith 9

Fetal-Maternal Endocrinology in Late Pregnancy:

Jonathan T. Lanman 11

Group Interchange

References 74

The Fetal and Placental Circulation in Late Pregnancy:

Geoffrey S. Dawes 81

Group Interchange

References 135

Index 141

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TABLE OF CONTENTS

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Geoffrey S. Dawes 81

Group Interchange

References 135

Index 141

THE JOSIAH MACY, JR. FOUNDATION CONFERENCE PROGRAM

DURING THE PAST FIFTEEN YEARS the Josiah Macy, Jr. Foundation has organized more than twenty conference groups, each group meeting for at least two days annually over a period of five or more years. Each meeting is limited to twenty-five participants (members and guests), selected to represent a multidiscipline approach to some urgent problem in the field of medicine and health. The goal of this conference program is the promotion of communication, the exchange of ideas, and the stimulation of creativity among the participants. The purpose of the publication of the transactions of the meetings is to share, as far as possible, the conference process with a larger audience than could participate personally in the discussions.

These conferences provide an opportunity for informal give and take among the participants. To further this purpose the number of presentations planned for each day is generally restricted to one or two. The member or guest selected to give such a presentation is requested not to "read a paper," but rather to highlight, in an informal manner, some of the more interesting aspects of his or her research, with the expectation that there will be frequent interruptions by participants in the form of questions, criticism, or comment. Such interruptions during the course of a presentation are encouraged and form an essential part of the "group interchange."

The conference program has always been viewed by the Foundation as an experiment in communication in which there is room for improvement and need for frequent reappraisal. Sufficient experience has already been gained to justify the conclusion that this type of conference is an effective way of improving understanding among scientists in medicine and allied disciplines, of broadening perspectives, of changing attitudes, and of overcoming prejudices. The further conclusion has been reached, as the result of this experiment, that the major obstructions to understanding among scientists lie in the resistance of human attitudes to change, rather than in difficulties of technical comprehension. Less extensive experience with non-scientists has indicated that the effectiveness of this type of conference is not limited to groups of scientists, but will function in any group meeting where more effective

communication is the primary goal. It is also clear that the same conference technique, with minor changes, is readily adapted to small international conferences.

The style of publication of the transactions has aroused considerable interest and some criticism. The criticism has been directed primarily to editorial permissiveness which has allowed in the final text, in some instances, too many questions, remarks, or comments which, although perhaps useful during a heated discussion, seem out of context and interrupt the sequence of thought in the printed volume. A few have objected to the principle of publishing in this style and would prefer a depersonalized summary without interruptions.

The Foundation Staff and the Scientific Editors of these volumes welcome criticism and hope to profit thereby in increasing the usefulness of the transactions to scientists and students of science in this country and abroad.

FRANK FREMONT-SMITH, M.D.
Medical Director

INTRODUCTORY REMARKS

Our hope, in arranging this conference, was to go as far afield as possible, even to the inclusion of men whose work comes no nearer to premature infants than, perhaps, fish, or worms, or even botany. We thought such a group of scientists could bring a completely new look to this subject, as some of us are so close to it that there is a tendency not to see it very well.

It is not necessary for this group to spend the first part of the conference discussing public health and obstetrical aspects of the problem or other topics to which the first part of a conference is so often devoted, because we have discussed them many times before.

We have selected the topics circulation and the glands of internal secretion as a logical starting place for our discussion, partly because of their importance and partly because of the presence of Dr. Dawes and Dr. Jost, who have many important contributions to make on these subjects.

Whatever controversy may arise concerning these aspects of prematurity will most likely remain unresolved at the end of our 3-day talks. Moreover such controversy will probably remain unresolved at the end of 5 years, but we hope that a little light may have been shed on the great territory of darkness that now exists.

Although there may not be much of a summary of our discussions at the end of the conference we hope that some synthesis will take place in the minds of those exposed to the ideas expressed here. We also hope that at the end of several years of meetings of this sort some conclusions will have been reached.

It is the purpose of these conferences to generate ideas to take home and think about.

CLEMENT A. SMITH, M.D.
Chairman

FETAL-MATERNAL ENDOCRINOLOGY IN LATE PREGNANCY

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IN DISCUSSING the fetal maternal endocrine relationships in late pregnancy, it may be helpful to divide them into those endocrine systems which tend to maintain, and then, at the appropriate time, terminate pregnancy, and those systems which are primarily directed at maintaining homeostasis while this process goes on. One of the reasons why the endocrinology of pregnancy is so difficult is that hormones of the first group, the estrogens, progesterone, and their trophic principles, which are primarily specialized growth hormones, show such striking species differences, even among closely related animals. One cannot apply what is known of one animal to another. Even such closely related rodents as the rat and the guinea pig are entirely different, as are long-term gestation mammals such as the horse and man.

Endocrine systems of the second group, which are primarily concerned with homeostasis, are more readily understood. Species differences are less striking, and in addition, pregnancy presents no serious problem for the mature endocrine system of the mother because even in the last month of pregnancy the total drain that the fetus imposes on the mother is insignificant. Even with such important items as nitrogen and calcium, the total amount transferred to the fetus in the entire last month of pregnancy, when the weight increment is the greatest, is only about 1 per cent of the store that exists in the mother. If there are distortions in homeostasis during pregnancy, it seems likely that they are imposed by the hormones of the first group. For instance, the fluid retention that commonly exists in pregnancy may be related to the production of progesterone, which has desoxycorticosterone-like action.

I should like to begin by discussing the adrenal relationships existing between the mother and fetus in pregnancy. Although the adrenal is primarily a homeostatic system in the adult, its function in the fetus is unknown and may be entirely different. The problem can best be summed up in Figure 1, which shows the growth curve of

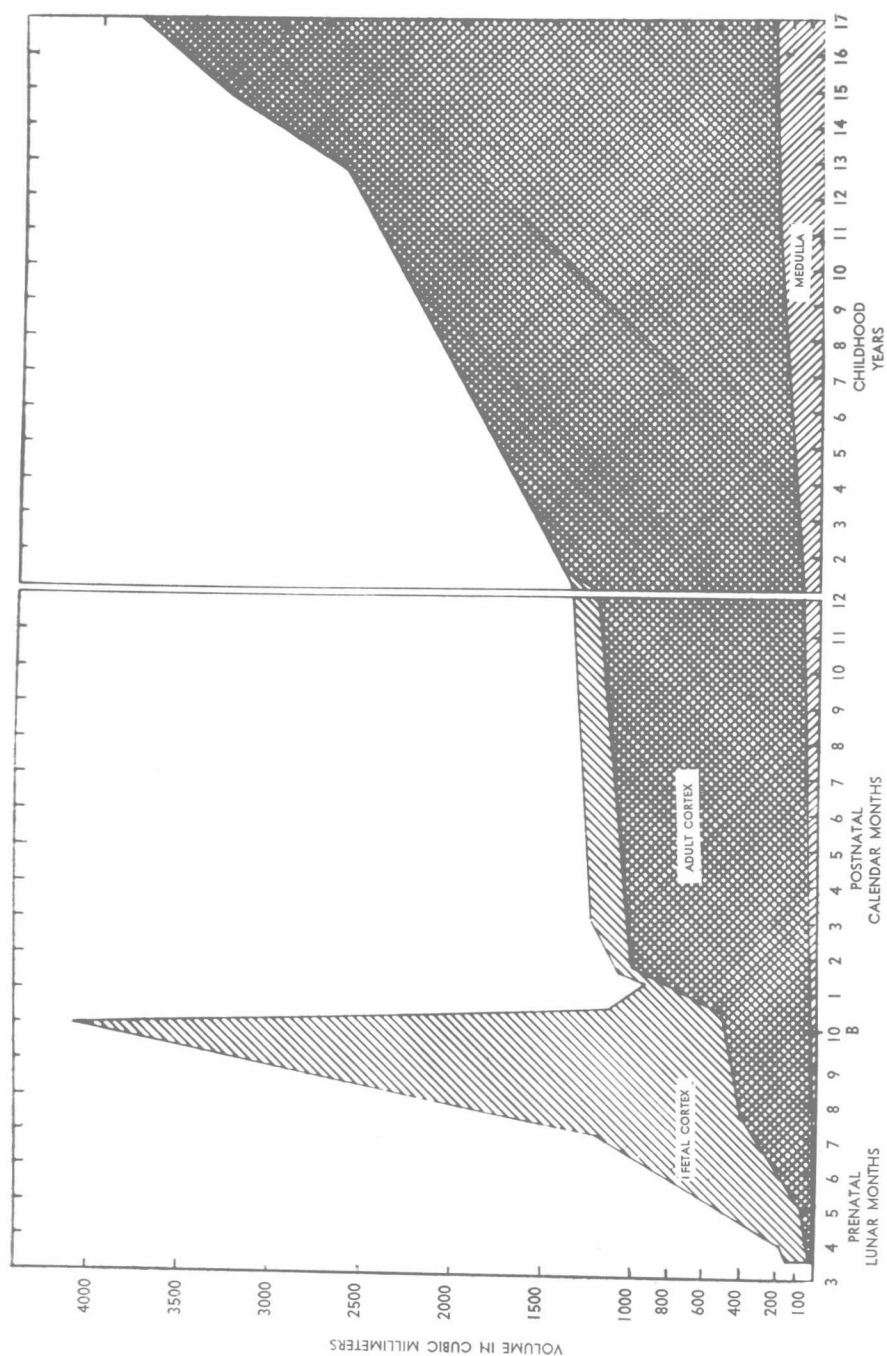


FIGURE 1. Growth of the supra-renal gland in the Negro. Reprinted, by permission, from Swinyard, C. A.: Growth of human supra-renal glands. *Anat. Rec.* **87**, 141 (1943).

the human adrenal gland during fetal life in the Negro. On the ordinate of Figure 1 is the volume of the gland in cubic mm., and on the abscissa is time. The diagonally shaded zone is the fetal zone of the human adrenal.

Parks: That is cortex?

Lanman: Yes. The central zone is the adult-type cortex, and the little wedge at the bottom is the medulla. During fetal life, the fetal zone grows very rapidly, and then abruptly at the termination of pregnancy it involutes and in 2 or 3 months is largely destroyed. This tissue, as far as we can be sure, does not reappear in later life. As the fetal zone involutes, the adult-type cortex grows rapidly. The fetal zone occupies about 80 per cent of the volume of the gland at birth, but during its disappearance, the fascicular zone grows rapidly, so that the net volume loss is only about 50 per cent. The problem is: What does this tissue do, why does it have this unique developmental pattern, and how can we find out more about it?

Hellman: Dr. Lanman, was there any reason for your selecting the Negro?

Lanman: Swinyard's (1) work was done in Negroes, and it is the best study that I know of. There is no similar study of white people but I believe the same course of events occurs.

Dawes: This was post-mortem material?

Lanman: Yes.

Dawes: Does the proportion between cortex and medulla change?

Lanman: It changes markedly. In the fetal adrenal it is rather difficult to find medulla; whereas the fetal cortex is at its peak. The medulla does not become prominent until after birth.

Dawes: But you do not have any systematic measurements?

Lanman: No, except for those on Figure 1.

Dawes: What is the evidence that in normal babies that have not died, the same rate of growth occurs?

Lanman: That is an almost unanswerable question, except in traumatic deaths. I know that in legal abortions that I have seen in Sweden, the fetal adrenals of normal fetuses are large and show the same histologic distinctions.

Fremont-Smith: In this period of involution, is this a frank necrosis of cells or do they merely cease to be regenerated?

Lanman: This is cell death, with necrosis, hemorrhage, phagocytosis, and collapse of the stroma on which the cells hang.