MEDICAL BULLETIN

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Two kinds of techniques have expanded the horizons of fetal endocrinology: those which permit the investigator to deprive the living fetus of an endocrine gland or glands and those which permit him to introduce hormones into the circulation of a fetus after the fetal adenoprivia has been accomplished.

By way of background, it appears probable that the developing endocrine glands begin to function during fetal life in utero. In trying to prove that this functioning occurs, however, technical difficulties arise. Hence the several lines of evidence, those already obtained and those to be sought, should be appraised with the following precepts in mind:

Any finding of a hormone in a developing gland would not necessarily mean that this hormone had been produced by the gland which contains it; nor would it indicate that the hormone leaves the gland and enters the blood. Perhaps it would be possible to determine whether the efferent blood of a developing gland contains more hormone than the afferent blood does. But even if this were demonstrated it would not show that the hormone exerts any physiological effect upon fetal or maternal target organs. In fact, relatively little is known about endocrine target organs during prenatal life.

Changes in presumptive target organs in the fetus have been produced by removing fetal glands and have been prevented by...
operating on the fetus and introducing into its body a hormone or hormones obtained from nonfetal sources. A desirable and convincing demonstration would consist of preventing such changes by means of grafted fetal gland or by means of introduced extracts of fetal glands, but this evidence will be difficult to obtain.

The experimental endocrinological study of the fetus entails two special conditions that are not usually encountered in ordinary endocrinology: the action of the placenta and the course of developmental changes. Since the placenta must continue to serve the fetus during any satisfactory experiment in vivo, the experiment should be designed to reckon with obscurities that might arise from the action of hormones of placental origin. The placental membrane probably allows certain hormones to pass freely from mother to fetus and from fetus to mother. It is problematical, though, whether this membrane permits certain other hormones to cross it to an extent that would have physiological significance.

Developmental change is an important element in the cumulative progression known as development of structure and function. This is qualitatively different from the recurring changes that are associated with metabolism during postnatal life. It presents complications because experiments performed at only slightly different developmental moments (periods) may yield different results. Since developmental moment is obviously related to age of fetus, the time of conception in the experimental animal should be known (by witnessed mating).

On the other hand, the rapidity of development is an experimental asset because it permits short experimental periods in certain species. An experimental period of 72 hours in the rat fetus, for example, is about one-seventh of the total period of gestation. This is equivalent to longer periods in those species with longer pregnancies.

**Techniques**

In indirect experimental approaches, testosterone propionate was injected into the amniotic sac of the monkey fetus. This hormone also was given to the monkey fetus via a series of intramuscular injections in the gravid female (Wells and van Wagenen).

In direct experimental approaches the fetal mouse was deprived of the thyroid or of the hypophysis in utero. The gland was destroyed by a narrow beam of x-rays. One disadvantage of this method is that other tissues in the path of the beam are likewise destroyed.
A method for subjecting the fetal rat to surgical adenoprivia and to the repeated subcutaneous injection of hormones has been devised and perfected at the University of Minnesota (Wells4,5). The fetus is surgically removed from the uterus in advance in such a manner that the placental circulation continues to function. After the fetal surgery or treatment or both, the experimental fetus is placed in the abdominal cavity of the mother, where it is nourished by the umbilical cord. The maternal wound is closed with sutures. Each time one of a series of subsequent treatments is to be made, the fetus is exposed again by reopening the maternal wound; the treatment is made, and the maternal wound is then resutured.

Many attempts in the Department of Anatomy to work out a satisfactory method for hypophysectomizing the fetal rat resulted in failure. Yet it was found possible to deprive the fetus of the hypophysis by decapitation (Wells6,7) and then to subject the headless fetus to a series of subcutaneous injections of hormone (Wells8). This locally devised method of hypophyseoprivia by decapitation is a useful experimental technique. It requires, however, special sets of controls in order to yield reliable evidence that any subsequent changes in the remaining fetal endocrine glands are consequences of the hypophyseoprivia itself, i.e., consequences of lack of hypophysis cerebri, as against lack of head. Colleagues in Iowa City,9 Chicago,10 and Paris,11 have also produced hypophyseoprivia by decapitating the fetus in utero.

Organ cultures in vitro represent another useful experimental approach. The developing reproductive tracts of fetal rats were removed and explanted onto clots of cock plasma and chick embryo extract.12 This method circumvents placental and maternal hormones. Male tracts and female tracts can be grown simultaneously on the same clot. Various combinations can be tested: tracts with gonads, tracts minus gonads, gonadless tracts plus crystals of hormones, etc.

TESTICULAR ANDROGEN

At the University of Minnesota, it has been virtually proved that in the fetal rat the developing testis produces an androgenic hormone which governs in part the development of the male accessory reproductive structures (Wells;13 Wells and Fralick;14 Wells, Cavanaugh, and Maxwell15). Castration reduced the number of prostatic buds, for example, and this effect was prevented by implanting a pellet of testosterone propionate under the skin of the castrated fetus. Similar observations have been reported in rabbit16 and mouse17 fetuses. It has not been possible to pre-
vent the effects of castration, however, by means of grafted fetal testis.18

TESTICULAR ANDROGEN AND SEX DIFFERENTIATION

Jost16 has reported that the castration of a male rabbit fetus of 19 days leads to the development of a female type of reproductive tract (one or two specimens); he has also stated that in a female rabbit fetus with a grafted testis in the right mesosalpinx, the right Wolffian duct persisted until the time of autopsy, i.e., shortly before expected parturition (one specimen). It has been pointed out that the number of Jost's specimens is small, that the observations are open to more than one interpretation, and that through the years the observations themselves have not been confirmed (Wells19,20). One may also speculate about what might have happened if these two or three rabbit fetuses had been permitted to live until maturity. In any event, Jost continued to rely heavily on these same specimens in advancing his version of a monohormonic theory of sex differentiation,21 namely, that the development of testes causes male differentiation in the male and that absence of testes in the female permits female differentiation. Several lines of scientific evidence have been advanced against Jost's monohormonic theory (Wells20).

HYPOPHYSIS-ADRENAL SYSTEM

It is known that pregnancy prolongs the life of adrenalectomized mammals22 and that it tends to relieve temporarily the symptoms of Addison's disease.23 Although the fetal adrenals have not been shown to be implicated in these phenomena, no observations seem to rule out the adrenal cortex of the fetus as a contributing factor. Progesterone of pregnancy seems to be involved, since either pseudopregnancy or injected progesterone are known to prolong the life of adrenalectomized animals.24 Moreover, it is possible that the fetal adrenals are sources of urinary ketosteroids in pregnant women with Addison's disease. Thus Samuels, Evans, and McKelvey25 have reported the case of a woman with Addison's disease which was temporarily relieved during the last three months of pregnancy, when the previously low level of urinary ketosteroids rose to 11-15 mg. per day; but after the child was born, the level immediately dropped to the original baseline, and the Addisonian symptoms fully returned.

At least seven lines of experimental evidence on the rat fetus from the University of Minnesota have indicated that the hypophysis produces a corticotrophic hormone, that this hormone
causes the adrenal cortex to produce cortical hormone(s), and that the functional relation between the hypophysis and adrenal cortex is reciprocal. These seven lines of evidence are as follows: a) hypophyseoprivia retarded the development of the adrenal;\textsuperscript{6,7,8,26a,26b,26c} b) this effect was prevented by subcutaneous injections of adrenocorticotrophin;\textsuperscript{8} c) unilateral removal of the left adrenal led to compensatory hypertrophy of the intact right adrenal;\textsuperscript{27} d) this effect was prevented by an implanted pellet of cortisone;\textsuperscript{27} e) in the normal fetus, a subcutaneously implanted pellet of hydrocortisone or of cortisone retarded the growth of the adrenal;\textsuperscript{28} f) implanted hydrocortisone also retarded the growth of the anterior lobe of the hypophysis;\textsuperscript{29} and g) bilateral adrenalectomy of the fetus apparently caused an enlargement of the anterior hypophysis in three litter-mate experimental-control pairs of fetuses.\textsuperscript{29}

These observations agree with results from other laboratories\textsuperscript{11,30} and with the results of other types of experiments. Thus, investigators have observed that hypophysectomy in the pregnant rat did not change the development of the fetal adrenals\textsuperscript{28,31} or of the hypophysis.\textsuperscript{29} The growth of the adrenals in the fetal monkey was reduced by giving corticotrophin to the pregnant mother;\textsuperscript{32} this effect presumably was due to an increase in maternal cortical hormone, and this hormone probably reached the fetal circulation by crossing the placental membrane.

**Hypophysis-Thyroid System**

For more than 30 years it has been known that the thyroid of a fetal pig of 9 cm. or more contains a substance (thyroid hormone) which will induce metamorphosis in the hypophysectomized tadpole and that the hypophysis of a fetal pig of 26 cm. or more contains thyrotrophin.\textsuperscript{33} Regarding man, perhaps future studies will clarify the report of a case of myxedema in which pregnancy relieved the symptoms and parturition was followed by reappearance of the symptoms.\textsuperscript{34}

Publications from the University of Minnesota record at least six lines of experimental evidence that in the rat the hypophysis-thyroid system begins to function before birth: a) fetal hypophyseoprivia retarded the growth of the follicle and the histologic development of the thyroid follicle;\textsuperscript{35,36} b) this effect was prevented by a series of four subcutaneous injections of thyrotrophin;\textsuperscript{36,37} c) injected thyroxin or injected triiodothyronine slowed up the development and growth of the thyroid;\textsuperscript{36} d) this effect was prevented by simultaneously injected thyrotrophin;\textsuperscript{36} e) fetal thyroidectomy seemed to speed up the cellular development of the anterior hypophysis;\textsuperscript{38} and f) in the nonthyroidecto-
mized fetus, injected thyroxin seemed to produce the opposite effect, namely, retarded cellular development of the anterior hypophysis. 38

These observations are interpreted to mean that the fetal hypophysis-thyroid system is largely independent of any hormones from the placenta and maternal hypophysis. This view is supported by the results of other workers who have found that in the pregnant female neither thyroidectomy 39, 40 nor hypophysectomy 40, 41 changed the growth of the fetal thyroid.

DIABETES AND PREGNANCY

Pregnancy in diabetic women presents serious complications and may lead to fetal abnormality and fetal mortality. In mothers who give birth to large babies manifest diabetes is likely to develop many years after delivery. It has been suggested that in a pregnant diabetic woman the hyperglycemia during the last half of the pregnancy damages the insulin-producing cells of the fetal pancreas and predisposes the infant to the subsequent development of diabetes. 42

In a study of subdiabetic patients, 43 women who showed an abnormal glucose tolerance during pregnancy and who were given insulin, the weights of their infants at birth were found to be smaller than those of the infants of control women who were not given insulin.

Experimental diabetes in pregnant rats has been investigated in continuing studies in the Department of Anatomy. 44-47

In a study by Kim and co-workers, 44 diabetes was induced by alloxan administration or by pancreatectomy either before conception or on the twelfth day of pregnancy. The diabetic rats usually were not treated with insulin; in the rats treated with insulin, the doses were deliberately kept at levels too low to control the hyperglycemia and glycosuria. In one group of rats, the insulin treatment was given only during the first 12 days of gestation and then stopped.

In pregnancies of normal rats and in those of diabetic rats, a positive correlation was noted between the neonatal weight and the length of gestation period. Regardless of the method of producing it, diabetes retarded the growth of fetuses as indicated by the fetal weights at 519 hours postcoitum. Since diabetes prolonged the gestation, the birth weight consequently approached the control level. In two litters of newborns from two mothers which were made diabetic before conception and were not given insulin, three of the 13 newborns (23 per cent) were regarded as “overweight newborns.” Each of these three weighed 7.9 gm. or more; 7.9 gm. was three times the standard
deviation in 289 newborns from 39 normal control mothers. Among these same 13 newborns, each of seven weighed 7.4 gm. or more; 7.4 gm. was two times the standard deviation in 289 newborns from control mothers. Pregnancies in diabetic rats were usually observed to be associated with high fetal mortality. Insulin treatment throughout the pregnancy prevented the prolongation of gestation and the retardation of fetal growth, but it did not reduce the fetal mortality to the normal level.

The insulin-treated diabetic animals with the greater fetal mortalities showed the lesser hyperglycemias and glycosurias.47 Perhaps the higher fetal mortalities were due in part to occasional hypoglycemics which had been produced by the injections of insulin.

Birth weight and fetal mortality were studied in pregnant subdiabetic rats which had received 25 or 30 mg. of alloxan injected intravenously on the twelfth day of the pregnancies.46 Associated with the subdiabetes was a statistically significant increase of 7.5 per cent in the birth weight. This increase occurred without any concomitant increase in the gestation period. In the 15 litters of newborns from 14 subdiabetic rats, two of the 132 newborns (1.5 per cent) were regarded as "overweight newborns." Each of these two weighed 7.9 gm. or more. Among these 132 newborns five weighed 7.4 gm. or more. Fetal mortality in the subdiabetic series was three times greater than that in the normal control series (18.7 per cent and 5.9 per cent, respectively).

Another study dealt with pancreatic islets and blood sugars in prenatal and postnatal offspring from diabetic rats and with beta granulation and glycogen infiltration (hydropic change).45 Fetal blood sugars were noted to be almost the same as maternal blood sugars in pregnant normal rats and also in pregnant diabetic rats. The blood sugar level in the neonatal offspring from diabetic mothers dropped to a normal level within 24 hours. Beta granules first appeared in the pancreatic islets of normal fetuses on the eighteenth day of gestation. Glycogen infiltration in the islet cells of fetuses from diabetic mothers appeared on the seventeenth day of gestation. Fetuses and newborns from mothers with blood sugars greater than 240 mg. per 100 ml. invariably showed glycogen infiltration and a decreased beta granulation in islets. Fetuses and newborns from mothers with blood sugar levels less than 175 mg. per 100 ml. showed normal beta granulation and absence of glycogen infiltration. At day 4 after parturition beta granulation increased, and at day 6 after parturition glycogen deposits disappeared. In the offspring from diabetic mothers hydropic change or glycogen infiltration oc-
curred in the beta cells but not in the alpha cells of the pancreatic islets. Thus, glycogen infiltration appears to be a sensitive indicator of beta cells; accordingly, an islet cell without beta granules but with deposited glycogen was regarded as a beta cell; the accuracy of our original observation was assured by our plan of studying two adjacent sections of pancreas, one stained by the aldehyde fuchsin method (stain for granules) and the adjacent one by the periodic acid-Schiff method (stain for glycogen, controlled by amylase digestion in control sections.)

*It is a pleasure to acknowledge the work of seven medical students who studied in our laboratories while this research was carried out: Sam Drage, Loren Anderson, Jerry Wright, Robert Wengler, Nancy Lund, Charles Drage and Donald Maus.

REFERENCES


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The Minnesota Maternal Mortality Study

J. L. McKelvey, M.D., C.M.†

A study of all maternal deaths in Minnesota has been carried out over a number of years. The findings and effects of this study are of primary importance to obstetricians, but because of its broader significance, this study is described here.

To a reasonable degree, the results of obstetric care are a measure of the effectiveness of all medical teaching and of the tools which have become available over the years. There are not many such measures. General mortality rates while a fair measure of the efficiency of medical care, are influenced by many other factors as well. Thus the control of infectious disease will be determined by the appearance of a single agent such as smallpox vaccination or antibiotics; it is a measure of the diligence of research activities. Mortality rates in childhood are more nearly measures of medical efficiency, but these too are affected by a number of other factors.

A number of other criteria, of course, could be used to evaluate medical efficiency. Information about these is most often lacking, since reports almost always come from large clinics and these reports are no expression of the effectiveness of the use of available knowledge on the general population. The reports from the teaching institutions, therefore, are likely to represent the skill of a specialized portion of the medical profession.

Obstetric efficiency, on the other hand, is a measure of the adequacy of the various assets of the average physician. Beyond his contributions as an investigator or teacher, the specialist can take little credit for improving obstetric mortality rates, since the vast majority of obstetric care in the state and in the country is in the hands of the general practitioner. Maternal

*This report was given at the Staff Meeting of the University of Minnesota Hospitals on December 11, 1959.
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mortality rates would appear, then, to measure his efficiency
and that of his teaching and tools.

While it is considerably more nebulous, one can scarcely
avoid the conviction that maternal mortality rates are also a
measure of the general sense of responsibility of physicians.
This sense of responsibility includes a great many things which
extend all the way from the amount of painstaking effort put
into patient care to seeing that adequate physical facilities are
locally available. This kind of responsibility is essential to mak­
ing available a high degree of technical skill. That this has been
achieved will be demonstrated in terms of declining maternal
mortality rates.

Our generation of physicians has been criticized for being
technicians as compared to other generations, who belonged
to what might be described as the "hand-holding school." Technicians or not, physicians of the present generation are
manifestly skillful in the application of medical care, partly
because of this sense of responsibility. This northwest region
has been fortunate, for no one can deal with the practitioners
of this area without recognizing in them an almost fierce sense
of pride in their work. While this can cause trouble from time
to time, one should remember that it is the source of a much
greater good.

How does one go about studying such a problem as maternal
mortality in a broad population? The Minnesota Maternal Mor­
tality study was set up in 1941. Largely through the efforts of
Dr. A. L. Dippel of the Department of Obstetrics and Gynecology, College of Medical Sciences. This resulted in the for­
mation of a special subcommittee of the Maternal Welfare Com­
mittee of the Minnesota State Medical Association. It was con­sidered essential that this activity be looked on as a project
undertaken by the doctors of the state themselves and not as
something imposed from without. A set of general principles and
minimum standards was agreed upon. It was clear that the
success of the project would depend mainly on the efficiency
with which complete information was obtained on all maternal
deaths. This requires that the investigators be skilled men,
psychologically fitted for dealing with a delicate problem and
unaffected by personal prejudice. The committee has been for­
tunate over the years to have the services of Dr. Donald Free­
man and Dr. Alex Baro; they have done a magnificent job and
have gradually assumed more and more of the task of collecting
and preparing the information. In the case of each known ma­
ternal death in Minnesota, they make a trip to the site of the
death and collect all the relevant data from the hospital and the physician. This information is then organized and presented to the Maternal Mortality Committee, which passes final judgment on diagnosis, deficiency or completeness of care, and responsibility for death. These conclusions are made part of the record, and a copy is sent to the physician concerned.

Cases are found by several means. A primary source is the death certificate; the Vital Statistics Bureau has been most cooperative and has matched all death certificates of women between 15 and 45 years of age with birth certificates. All sorts of other sources, including personal reports and newspapers, have turned up useful information. That death certificate information alone is inadequate is manifested by the fact that as much as 30 per cent of the case material has come from other sources. It is now thought that for practical purposes all cases are being found, with the possible exception of an occasional death from abortion, which for one reason or another the physician or the hospital wish to hide. Even some of these deaths have been found.

The maternal mortality figures ordinarily given are based on a detailed description produced by the U. S. Bureau of the Census. This information is obtained from death certificates. An attempt is made to translate the brief diagnosis on the death certificate into what are called obstetric and nonobstetric deaths. The latter are simply excluded from the reckoning, a procedure that leaves much to be desired. If the physician neglects to list an associated pregnancy, it is unlikely to be caught. (This has actually happened with a University Hospitals death certificate.) If the physician wishes to hide the obstetric association, he can readily do so. The Minnesota Maternal Mortality Study has dispelled the assumption that the diagnoses on the death certificates have a reasonable relation to reality. Indeed, one might justifiably conclude that any study based on death certificate diagnoses is more likely to be wrong than right. This is particularly true of such a diagnosis as coronary occlusion, in which purposeful falsification has been encountered. There is simply not enough accurate information on the death certificate to allow a conclusion as to whether death was due to obstetric or nonobstetric causes. In Minnesota, the Vital Statistics Bureau and the State Health Department have over the years leaned more and more heavily on the Maternal Mortality Study for this kind of information, and the reports in Minnesota are now probably more accurate than those of other states where the use of death certificates is the usual method of collecting and reporting maternal deaths. The number of women reported to
have died during pregnancy or the ensuing three months of obstetric causes is given for every 1,000 or 10,000 live births in the area.

Comparisons between one geographic area and another, and particularly between one country and another, are clearly inaccurate except in the broadest sense. Using the same standards within the same geographic area, however, changes observed from year to year are probably significant. It would be helpful if all maternal deaths, both obstetric and nonobstetric, were reported, following which so-called nonobstetric deaths could be deducted.

The Minnesota Maternal Mortality Study reports two figures. All deaths during pregnancy and the subsequent three months from whatever cause are reported as a gross figure. On the basis of detailed information, nonobstetric deaths are excluded, although these have often been classified arbitrarily. Obstetric deaths are reported as a separate figure. Neither of these figures coincides with the Minnesota State report for several reasons, one of which is that the two use different twelve month periods for the year.

Figure 1 shows the maternal mortality rates for the United States and for Minnesota since 1915. Two features stand out: The maternal mortality rates of the earlier years were dreadful. During some of these years, only one other reporting country in the world had a worse record. The second feature, of course, is the remarkable drop since the mid 1930’s to a level which our predecessors would have considered impossible. If this be a measure of the efficiency of the practicing physician in general, it is not only good—it is wonderful!

Table 1 shows in greater detail what has happened in Minnesota during the years of the Maternal Mortality Study. There has been a continuous drop in the gross maternal mortality rate, which includes deaths of women during pregnancy and the subsequent three months from all causes. In 1957, only 60 maternal deaths occurred (11 of them due to Asian influenza), for a rate of 0.70 per 1,000 live births. The mortalities ascribable to obstetric causes have also fallen over the years. In 1957, there were 21 obstetric deaths for a rate of 0.24. Most gratifying of all is the drop in those obstetric deaths that were considered by the committee to be preventable. In 1957, there were seven preventable deaths, of which six were the responsibility of the physician and one, the responsibility of the patient; this is a preventable death rate of only 11.7 per cent. This has to be compared with a 73 per cent preventable rate in 1941. Whatever “hand holding” may have been lost, the “tech-
Fig. 1. Maternal Mortality rates per 10,000 live births for Minnesota and the United States since 1915.
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TABLE 1
MINNESOTA MATERNAL MORTALITY RATES AND PREVENTABILITY
1941, 1950-1957

<table>
<thead>
<tr>
<th>Year</th>
<th>Live Births</th>
<th>Maternal Deaths</th>
<th>Total Gross Mort. per 1,000 Live Births</th>
<th>Obstetric Corrected Mort. Rate</th>
<th>Preventability % of Total Mat. Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1941</td>
<td>55,293</td>
<td>112</td>
<td>2.03</td>
<td>1.68</td>
<td>82</td>
</tr>
<tr>
<td>1950</td>
<td>76,074</td>
<td>68</td>
<td>0.89</td>
<td>0.62</td>
<td>22</td>
</tr>
<tr>
<td>1951</td>
<td>80,099</td>
<td>57</td>
<td>0.71</td>
<td>0.45</td>
<td>24</td>
</tr>
<tr>
<td>1952</td>
<td>78,990</td>
<td>58</td>
<td>0.73</td>
<td>0.39</td>
<td>10</td>
</tr>
<tr>
<td>1953</td>
<td>79,362</td>
<td>59</td>
<td>0.74</td>
<td>0.42</td>
<td>15</td>
</tr>
<tr>
<td>1954</td>
<td>81,033</td>
<td>40</td>
<td>0.49</td>
<td>0.33</td>
<td>12</td>
</tr>
<tr>
<td>1955</td>
<td>81,665</td>
<td>43</td>
<td>0.53</td>
<td>0.38</td>
<td>8</td>
</tr>
<tr>
<td>1956</td>
<td>82,620</td>
<td>45</td>
<td>0.54</td>
<td>0.31</td>
<td>10</td>
</tr>
<tr>
<td>1957</td>
<td>86,019</td>
<td>60</td>
<td>0.70</td>
<td>0.24</td>
<td>7</td>
</tr>
</tbody>
</table>

nicians" seem to be doing an efficient job in Minnesota.

This study has accomplished many things of value. It has changed the stress in teaching. Unidentified cases are used for teaching undergraduates, and most of this teaching is now done by the two investigators themselves. A great deal of the problem of preventable maternal deaths lies in the mishandling of simple things: Simple lack of adequate examination, simple lack of laboratory information, and the mishandling of blood, electrolytes, and fluids account for a surprisingly large proportion of trouble. The teacher with his interest in disease processes tends to pass over such things lightly. They are now being stressed.

Furthermore, certain trouble areas in the state have been found. The study showed, surprisingly, that most of the deaths due to placenta previa were coming from one area, where the prevailing view was that accouchement forcé was proper treatment for this condition; this misconception was gently handled. It was found that one technician had been responsible for three deaths from mismatched blood, and this was handled somewhat more stringently. The proportion of preventable deaths is still considerably higher in rural than in urban areas, and an attempt is presently being made to change this problem.

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This study has a significant educational value for the individual physician. In many of the cases of preventable death, the physician is confused about what has actually taken place. After he has given details to the investigator and has had the committee report, much of his confusion is dispelled. All of this is a potent stimulus to improved records and care.

The study has also supplied useful information for talks to local medical societies. We now have data as to what has been wrong and what can be improved, and what specific problems need discussion in certain areas. The hospitals where bad obstetrics is being practiced have been pinpointed. This has already led to a number of improvements.

The meetings of the committee have been magnificent "dry" clinics, for the members have pointed up a number of things. There was, for example, only a vague recognition of the significance of the strange pulmonary edema of pregnancy. The significance of the disastrous effects of arteriolosclerotic toxemia of pregnancy has been made clear. As a result of the study, the importance of deaths resulting from anesthesia has suddenly become obvious, and, accordingly, anesthetic procedure was changed in at least two hospitals. All kinds of rare problems are concentrated in the case material which passes through the committee's hands.

The effect of the committee's activities on the practice of obstetrics in the state is not absolutely clear. But the physician does know that if he has a maternal death, someone will be around to look into the details. There is at least a strong suggestion that this fact has helped improve records, increase consultations, and add to the technical care in handling patients.

Finally, it has become evident to the committee that, at least by comparison with previous accomplishment, further improvement is limited. Some figure a little lower than 0.2 per 1,000 appears to be the rational lower limit of obstetric deaths, and the rate in Minnesota in 1957 was 0.24 per 1,000 live births. Thus the committee members are beginning to turn their thoughts to other problems. The possibilities of reducing fetal and neonatal risks and damages and of studying the effects of obstetric adventures over periods longer than the three months after delivery are intriguing. It might also be useful to examine the causes of obstetric damages as distinct from obstetric mortalities. The Maternal Mortality Study is making it evident that some such redirection of activities is needed.
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Conclusions

1. The nature and accomplishments of the Minnesota Maternal Mortality Study have been described.

2. Maternal mortality has dropped remarkably in Minnesota and in the entire nation. In Minnesota, in fact, the present rate is approaching what might be considered an irreducible minimum.

3. It is suggested that these findings can be interpreted as a measure of the efficiency of the medical group as a whole. If this be so, medical care in the Northwest is remarkably efficient and the general practitioners in particular are a skilled and responsible group.

MINNESOTA MEDICAL FOUNDATION

1939
NEUROLOGY

Dr. Maynard Cohen, Professor, was awarded a $14,171 research grant by the Minnesota Multiple Sclerosis Society. He was also awarded equal extensions of the grant for the next two years, contingent upon public support of the Society’s fund drive. Dr. Cohen is chairman of the Society’s southeastern Minnesota medical advisory committee.

SCHOOL OF PUBLIC HEALTH

Dr. Stewart C. Thomson, Professor and Associate Director, delivered the convocation address Nov. 19 at the 11th annual College Health Day program at the University of Nebraska, Lincoln, Neb. He spoke on “Health Facts, Fads, and Fallacies.”

PHYSICAL MEDICINE AND REHABILITATION

Dr. Glenn Gullickson and Mr. Robert A. Walker of the department represented the University of Minnesota Rehabilitation Center Dec. 4-8 in New York City at the annual meeting of the Conference of Rehabilitation Centers and Facilities. Dr. Paul M. Ellwood, Clinical Associate Professor of Pediatrics at the Medical School, was elected President of the Conference at the meeting.

Marcia Galbraith, OTR, has joined the staff, and Kay Smith, RPT, and Sue Swenson, RPT, have resigned.

Dr. Glenn Gullickson and Mrs. Gullickson are parents of a baby girl born Dec. 11, 1959. She was named Mary Margaret.

CANCER BIOLOGY

Dr. John J. Bittner, Professor and Head of the Division, addressed a meeting of the New York Cancer Society, New York City, on Dec. 8. He discussed the topic “Inherited Hormonal Patterns and Mammary Cancer of Mice.” Dr. Clarence Dennis, former member of the Department of Surgery at the University of Minnesota Medical School, and who is now head of the New York State Medical School in Brooklyn, N.Y. is a member of the Society.

INTERNAL MEDICINE

Dr. Wesley W. Spink, Professor, spoke on “The Education of a Doctor” on Oct. 2 at a regional meeting of the American College of Physicians in Billings, Mont. On Oct. 23 he lectured as a Visiting Professor at St. Luke’s Hospital, St. Louis, Mo.
LABORATORY OF PHYSIOLOGICAL HYGIENE

Dr. Ernst Simonson has been awarded a grant of $6,662 by the U. S. Public Health Service for research in the aging of nervous functions in relation to stress. His award was one of 71 totalling $1,751,270 made during December which will aid investigators in 21 states on the biological, psychological, and sociological aspects of aging.

SURGERY

Dr. Alan Thal, Assistant Professor, gave the Ciba Memorial Lecture at the University of Vancouver, British Columbia, on Nov. 30. The title of his talk was “Pancreatitis, Clinical and Experimental Aspects.”

BACTERIOLOGY and IMMUNOLOGY

“The Immunoelectrophoretic Characterization of Agammaglobulinemic States” was the title of a paper delivered by Dr. Robert A. Bridges, Assistant Professor, Nov. 6 in Chicago, Ill. at the 32nd annual meeting of the Central Society for Clinical Research. Dr. Robert A. Good, Professor of Pediatrics, was a co-author, and is an editorial board member of the Society’s journal, THE JOURNAL OF LABORATORY AND CLINICAL MEDICINE.

PHYSIOLOGICAL CHEMISTRY

Dr. David Glick, Professor, lectured Dec. 11 at the Research Division of Smith, Kline and French Laboratories in Philadelphia, Pa. His topic, “Quantitative Histochemical Studies on the Adrenal Glands in Various Functional States” was a review of research carried out during the past few years in the histochemical laboratory which he directs.

PEDIATRICS

Dr. Robert Vernier, Assistant Professor, presented a paper titled “The Pathogenesis and Pathology of Anaphylactoid (Henoch-Schönlein’s) Purpura” Nov. 7 before the Central Society for Clinical Research in Chicago, Ill. Co-authors were Drs. Howard G. Worthen, Instructor, and Eleanor Colle, Assistant Professor.
THE MEDICAL BULLETIN

DEATHS

Dr. Albert Canfield (Med. '43) died Nov. 24, 1959 in Madison, Wisconsin. Death was caused by hypertensive heart disease at age 43. He specialized in internal medicine and was a former resident of Minneapolis.

Dr. Donald L. Olson (Med. '51) was killed Dec. 13, 1959 in an automobile accident near Moorhead, Minn. He was 38 years old and was in practice as an orthopedic surgeon in Fargo, N.D. He is survived by his wife and six children.

Dr. Paul A. Peterson (Med. '51) died Dec. 27, 1959, as the result of injuries suffered in the auto accident which killed Dr. Donald L. Olson, his companion. He was 34 years old and is survived by his wife. Dr. Peterson practiced in Fargo, N.D. He interned at Ancker Hospital, St. Paul, Minn.

Memorials

Recent memorial contributions to the Minnesota Medical Foundation have been received in memory of:

Mrs. Etta Salinger
Dr. E. A. Cary
Mr. Anthony Thiel
Mrs. H. P. Leavitt

Mr. Fred E. and Mrs. Anastasia Hodgson

Memorial gifts are a practical means of honoring the memory of a friend or loved one while providing needed assistance for the University of Minnesota Medical School. Dignified acknowledgments are made by the Foundation to both the donor and to the family of the deceased.
CONSTRUCTION UNDERWAY AT MEDICAL SCHOOL

Construction of Diehl Hall (below), the University's new bio-medical library building, continues through the winter with date of occupancy now estimated for October 1960. The $2.5 million structure rising next door to the University Hospitals will have three floors to provide badly needed medical library facilities. It will also have two floors below ground level which will house research laboratories for certain clinical departments. Named for the Medical School's dean Emeritus, Harold S. Diehl, it will add 45,000 square feet of critically needed research and study space to the University of Minnesota Medical Center. Funds for the project were provided by the University of Minnesota, Minnesota legislature, U. S. Public Health Service, and generous donations of private individuals and firms. The view of the construction zone is looking east from the roof of the Mayo Memorial building.
The Jackson-Owre Hall addition to the medical center facilities (above), located at the southwest corner of the basic sciences quadrangle, will be completed during the summer of 1960. It will be shared by the Medical School and the School of Dentistry. The Medical School's half will provide research space for the Departments of Anatomy and Pathology, and release current research space in Jackson Hall for additional classroom space. Budgeted at over $1,000,000, the Jackson-Owre addition was made possible by Minnesota legislative appropriation and a U. S. Public Health Service matching grant. Jackson Hall, home of the Anatomy and Pathology Departments, will soon be remodeled, and Millard Hall, site of the Departments of Physiology, Physiological Chemistry, and Pharmacology, is now undergoing extensive internal repairs.
## MINNESOTA MEDICAL FOUNDATION

### STATEMENT OF CONDITION

As of September 30, 1959

#### ASSETS

<table>
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<th>Description</th>
<th>1959</th>
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<td><strong>Current Funds</strong></td>
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<tr>
<td>Investment, U. S. Gov't Bonds</td>
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<td><strong>Endowment Funds</strong></td>
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<tr>
<td>Cash in Bank—Checking</td>
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<td>Investment, University of Minnesota</td>
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<td>40,556.86</td>
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<td><strong>TOTAL ASSETS</strong></td>
<td>$115,969.95</td>
<td>$ 87,636.05</td>
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### NOTES GROWTH IN 1959

An audited account of Minnesota Medical Foundation’s financial progress during 1959 is published above for your information. Total assets of the Foundation advanced more than $28,000 during the year, and on Oct. 1, 1959 stood at nearly $116,000—the highest since the Foundation was established twenty years ago.

In addition to normal income and expenditure, some simple adjustments of accounts were made which helped put Foundation funds to work more effectively. The Finance Committee, headed by Mr. Malcolm B. McDonald, is planning further adjustments in 1960 which are calculated to return maximum interest on assets held by the Foundation.

Progress in 1959, however, goes beyond the financial picture presented here. In the past year the Minnesota Medical Foundation fashioned a partnership with the University of Minnesota which affords coordination of the Foundation’s work with that of the Greater University Fund, the general fund raising channel of the institution.

A full time Executive Secretary, first in Foundation history, was engaged, and given collateral responsibility as an associate director of the Greater University Fund. He thus becomes responsible for all
The Minnesota Medical Foundation, under full time direction for the first time, looks forward to substantial enlargement of its service to the Medical School.

An improved University of Minnesota MEDICAL BULLETIN is now being published under Foundation supervision, and a Foundation committee is already at work preparing the MEDICAL BULLETIN for a vastly more important role in the future development of the Foundation.

A membership committee is planning an intensive campaign for more members in 1960, and a fund raising committee will soon begin soliciting major financial gifts from private foundations, corporations, and individuals. Meanwhile, the existing Foundation programs will continue.

Officers of the Foundation are constructing a master plan for Foundation programming during the next five years. The potentials are exciting to ponder.

I believe you will want to follow closely the growth of the Minnesota Medical Foundation during the coming months and years. There is every reason to believe its success will justify the belief of the visionary Board of Trustees which foresaw its great possibilities.

—Eivind Hoff, Jr.
Executive Secretary

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MINNESOTA MEDICAL FOUNDATION

STATEMENT OF CONDITION
As of September 30, 1959

<table>
<thead>
<tr>
<th>LIABILITIES</th>
<th>1959</th>
<th>1958</th>
</tr>
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<td>Undesignated Funds</td>
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<td></td>
<td>$ 44,880.86</td>
<td>$ 43,603.86</td>
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<tr>
<td>TOTAL LIABILITIES</td>
<td>$115,969.95</td>
<td>$ 87,636.05</td>
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</table>

*Audit by Theodore Stark & Co., Certified Public Accountants, Minneapolis, Minn.*
Alumni Notes

♦ 1919

Hyman S. Lippman is Director of the Wilder Child Guidance Clinic, St. Paul.

♦ 1923

Harold G. Reineke, formerly of New Ulm, Minn. was named President-elect of the American Roentgen Ray Society at its 60th annual meeting Sept. 25 in Cincinnati. He is now Professor of Clinical Radiology at the University of Cincinnati Medical School. His father was a pioneer physician at New Ulm.

♦ 1924

Frederick N. Grose and Mrs. Grose recently celebrated their 25th wedding anniversary. The community of Clarissa, Minn., where Dr. Grose has practiced for many years, joined in honoring the couple.

Arild E. Hansen is now Director of Research at the Bruce Lyon Memorial Research Laboratory of the Children's Hospital of the East Bay, Oakland, Calif. He was formerly on the staff of the University of Texas Medical School, Galveston, Texas. In his new post he succeeds his former teacher, Dr. Irvine McQuarrie, Professor Emeritus of Pediatrics.

A. B. Rosenfield of the Minneapolis Department of Health was elected president of the Minnesota Public Health Conference for 1960.

♦ 1925

H. Milton Berg, Bismarck, N.D. physician, was named President-elect of the Radiological Society of North America. The society is the largest scientific radiological group in the world.

Glen W. Tuttle writes from Kimpese, Belgian Congo, where he practices general medicine with emphasis on obstetrics and gynecology. He teaches at the Institute of Medical Evangelists and serves as medical director of an international interdenominational mission hospital and training school. Dr. Tuttle's family now includes a wife, two sons, and two daughters.

♦ 1927

Summer S. Cohen, Minneapolis Internist and Phthisiologist, addressed the November meeting of the St. Louis County Medical Society.
Miland E. Knapp was keynote speaker at the Michigan Rehabilitation Conference held Sept. 27-29, 1959 in Traverse City, Mich. He spoke on "Research in Rehabilitation."

Capt. Stewart W. Shimonek, Medical Corps, U. S. Navy, has assumed new duties as assistant district medical officer and permanent medical member of the Physical Evaluation Board for the Fifth Naval District, Norfolk, Va. He was formerly stationed at Corpus Christi, Texas.

Herman E. Drill, Hopkins, Minn. is president of the Minnesota Medical Foundation and the Hennepin County Tuberculosis Association.

Raymond L. Gregory is Professor of Internal Medicine; Director of the John Sealy Memorial Clinical Research Laboratory; Director of the Endocrine Clinic; and physician at the University of Texas Medical Branch hospitals, Galveston, Texas. His research is in metabolic and endocrine diseases and experimental hypertension.

Marland R. Williams is now established in a newly-completed Medical Arts Building in Cannon Falls, Minn.

Harold R. Hennessy is manager of the full time staff of the American College of Surgeons headquarters at Chicago, Ill. He was recently elected to membership in the Order of Lafayette, (a military society of American and French officers). Dr. Hennessy's family includes his wife, one son, and three daughters.

Paul N. Larson was elected chief of staff at Northwestern Hospital, Minneapolis. He is a Fellow of the American College of Surgeons and specializes in obstetrics and gynecology.

Earl Barrett, Duluth, presented a paper on rheumatic fever at a staff meeting of the Divine Infant Hospital, Wakefield, Mich., Nov. 19. Two colleagues, William Martin ('41) and J. F. Schmid ('43), spoke on the same occasion.

Duane C. Olson, formerly of Gaylord, Minn., is now engaged in the general practice of medicine with Drs. Kenneth V.
Hodges and Kristofer Hagen at the Southdale Medical Building in Minneapolis.

♦ 1939

William B. Stromme, Minneapolis surgeon, presented a paper at the 45th annual clinical congress of the American College of Surgeons in Atlantic City in September. His topic was "Intrauterine Fetal Deaths in the Second Trimester."

♦ 1940

Lt. Col. Ivan C. Dimmick assumed duties as post surgeon at Ft. Sam Houston, Texas. Devoting his entire medical career to the U.S. Army since 1940, Col. Dimmick was recently on assignment as medical advisor to the Imperial Iranian Army in Teheran, Iran. He is a native of Benson, Minn., is married, and has four children.

Ralph Papermaster, Two Harbors physician, was elected president and chief of staff at the Lake View Memorial Hospital in that city.

♦ 1941

Merrill E. Henslin is in general practice at a clinic in Santa Ana, California. He is married, has one son, and is a member of the American Academy of General Practice.

♦ 1942

Kristofer Hagen leaves his Minneapolis practice this month to operate a mission hospital in a remote section of northeast India. He will serve until at least late 1962 as superintendent of Mohulpahari Christian Hospital in Santal Parganas district of Bihar state. The area is 150 miles north of Calcutta and at least 20 miles from the nearest railroad. Dr. Hagen will take his wife and two daughters with him. He is also an ordained Lutheran minister, and will turn his local medical practice over to his associates in Southdale Medical building until his return.

♦ 1943

V. Richard Zarling and Mrs. Zarling, Minneapolis, are the parents of a daughter, Teresa, born Sept. 7, 1959.

♦ 1945

Harvey A. Knoche is now practicing in Gaylord, Minn., where he took over the practice of Dr. Duane C. Olson (Med. '37). Dr. Knoche has been a physician in Morgan, Minn. for several years.
1946

James A. Cosgriff, Jr., Olivia, Minn., attended the European Rheumatologic Congress in Istanbul, Turkey, and toured Italy and Switzerland during a visit abroad in 1959.

1950

John Patrick Moran is on the staff at the University of Texas Medical Branch, Galveston, Texas, as an Instructor in Otorhinolaryngology.

1953

Charles Sherman Hoyt is now in the practice of pediatrics with Drs. Albert Schroeder, Hreidar Agustsson, and Detlof Olson at the Southdale Medical Building in Minneapolis. He received his training in pediatrics at the Mayo Clinic.

Robert W. Gustafson is now affiliated with Drs. E. E. Zemke and Robert Schulz in the practice of medicine at Fairmont, Minn.

1955

James W. Sipe and Mrs. Sipe announce the birth of a son, Michael John, on Sept. 26, 1959. They are residents of Coon Rapids, Minn.

Richard Eddy has joined the Alexandria Clinic, Alexandria, Minn. in the practice of medicine following internship in Sacramento, Calif., and a tour of duty with the U. S. Army.

1956

Capt. Roger E. Linnemann was commended by the U. S. Army for outstanding performance of duties as a medical officer at the Army hospital in Landstuhl, Germany, for the past two years. He is formerly of St. Joseph, Minn. His wife, Yvonne, is with him in Germany.

1958

Wendell P. Enggelstad, formerly of Duluth, has joined Drs. J. S. Siegel and Wayne Johnston in practice at Virginia, Minn.

Capt. Howard L. Schochet recently completed the military orientation course at Brooke Army Medical Center, Ft. Sam Houston, Texas. He completed his internship at Ancker Hospital, St. Paul.
Floyd J. Swenson is in a private practice in Cook, Minn., as an associate of the Lenont-Peterson Clinic at Virginia, Minn. He completed his internship at the U.S. Public Health Service Hospital, Seattle, Wash.

Lt. Robert A. Olson is now on duty with the Navy at Pensacola, Fla. He is taking advanced training in the Medical Corps.

Lt. Clark A. Shattuck has been assigned to duty at the U.S. Navy Aviation Facility Examination Station, Houston, Texas.

Lt. Richard H. Hedenstrom, Medical Corps, U.S. Navy, has qualified as a flight surgeon following advanced training at the Naval School of Aviation Medicine, Pensacola, Fla., and has been transferred to duty with a helicopter antisubmarine squadron.

1959

Carl E. Christenson, now interning at Bethesda Hospital, St. Paul, will begin private practice at Clinton, Minn. later this year.

Editor's Note: The MEDICAL BULLETIN invites your contributions to the Alumni Notes column. Send your news to The Editor, UNIVERSITY OF MINNESOTA MEDICAL BULLETIN, 1342 Mayo Memorial, University Campus, Minneapolis 14, Minnesota. Personal news welcome.
Coming Events

University of Minnesota Medical School

Courses in Continuation Medical Education During 1960

January 21-23 . . . Surgery for Surgeons
February 8-10 . . . Cardiovascular Diseases for General Physicians and Specialists
February 15-19 . . . Pediatric Neurology for Specialists
February 29-March 2 Pediatrics for General Physicians
March 14-16 . . . . Internal Medicine for Internists
March 19 . . . . . . Trauma for General Physicians
March 28-April 1 . . Endocrinology for General Physicians
April 7-9 . . . . . Emergency Surgery for Surgeons
April 11-13 . . . . Radiology for General Physicians
April 21-23 . . . . Otolaryngology for General Physicians
May 2-6 . . . . . Intermediate Electrocardiography for General Physicians and Specialists
May 16-18 . . . . Office Psychotherapy for General Physicians
May 23-27 . . . . Proctology for General Physicians

Courses are held at the Center for Continuation Study or at the Mayo Memorial Auditorium on the campus of the University of Minnesota. Usual tuition fees are $10 for a one-day course, $40 for a three-day course, and $65 for a one-week course. These are subject to change under certain circumstances.

Register early. For further information write to:

DIRECTOR
DEPT. OF CONTINUATION MEDICAL EDUCATION
1342 Mayo Memorial — University of Minnesota
Minneapolis 14, Minnesota
Join the Minnesota Medical Foundation Today!