

Diabetes Mellitus and Pregnancy

Further Experience with Control of Perinatal Fetal Mortality

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The management of the diabetic patient during pregnancy continues to be a challenge and a subject of great interest, both to the obstetrician and the internist. Improved regulation of diabetes restored the regularity of ovulation and has expanded the number of young patients who live through the reproductive years. Thus, it is estimated that there are 80,000 diabetic women of childbearing age in the United States, and that 50,000 juvenile diabetic subjects are or soon will be potentially childbearing.¹ According to the studies of the Chicago Lying-In Hospital and the Boston Lying-In Hospital, the incidence of deliveries of diabetic patients in large maternity hospitals is one in 1,000.²

Medical institutions around the world continue to report their individual statistics. The data from The Johns Hopkins Hospital on pregnancies in diabetic subjects observed during the eleven-year period from 1942 through 1952 have been reported;³ included was information on fifty-six pregnancies handled by the same technics utilized in this study. Presented below are data on pregnancies in diabetic subjects occurring during the subsequent six-year period.

MATERIAL AND METHODS

From Jan. 1, 1953, to Dec. 31, 1958, there were ninety-seven deliveries in eighty-five diabetic patients at The Johns Hopkins Hospital. Of these, forty deliveries occurred in white patients and fifty-seven in nonwhite patients. This ratio is similar to that of the previous report. The group included patients of both clinic and private status, the latter group comprising a small minority. Most of the clinic patients had been followed at the hospital's prenatal diabetes clinic during the last two trimesters of their pregnancy. A few had been followed at county clinics prior to their hospital admission for delivery. There were others who came to the hospital for delivery without prenatal care, and others still who

came to the prenatal clinic very late in pregnancy.

As in the previous report,³ only cases in which the diagnosis of diabetes was certain were included in the series. The criterion for the diagnosis of diabetes was the finding before or during the pregnancy of two or more fasting blood sugar levels above 130 mg. per 100 ml. as measured by the Folin-Wu technic⁴ or in excess of 115 mg. per 100 ml. as measured by the glucose oxidase method.⁵ A glucose tolerance test, employing 100 gm. of glucose, was performed on subjects suspected of manifesting a very mild form of diabetes; the results were interpreted by standard criteria.⁶

The eight pregnancies in private patients were supervised by members of the private visiting staff—an internist, and an obstetrician; the latter conducted the delivery. Clinic patients were delivered by members of the hospital house staff. Clinic patients were followed at the prenatal diabetes clinic, supervised by an obstetrician (WNL) and an internist (PHF). There the patients were seen at intervals of one to two weeks. Certain patients were seen in consultation by an ophthalmologist for an evaluation of possible progression of vascular disease. Measurement of fasting blood glucose and urinalysis were performed at the time of the return visits. During the intervals, the patients examined their urine for sugar before each meal.

An effort was made to regulate the diabetes as strictly as possible, to maintain the fasting blood sugar below 130 mg. per 100 ml. as measured by the Folin-Wu method and to avoid reactions or great swings in blood sugar levels throughout the day. A diet was prescribed offering each day 150 to 250 gm. of carbohydrate, 100 gm. of protein, and the balance of calories as fat, usually in amounts of forty to ninety grams. Effort was made to reduce the weight of obese women during their pregnancies. Crystalline, Protamine-Zinc, NPH and, more recently, Lente insulin were employed. An occasional patient needed no insulin. None of the oral hypoglycemic compounds was used. Estrogens and progesterone-like drugs were not employed.

The majority of patients were admitted to the hospital for regulation of their diabetes over a short period

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at some stage of their pregnancy. At the thirty-seventh week of gestation, or before if indicated, the appropriate type of delivery and the possible need for early delivery were reviewed. If the diabetes mellitus was mild, the pregnancy uncomplicated, and the fetus estimated to weigh between 3,000 and 3,400 gm., the patient was allowed to deliver vaginally. In this group of mildly diabetic subjects, if the uterine cervix was favorable, labor was induced at the end of the thirty-seventh week, by stripping and rupturing the membranes. If the condition of the uterine cervix was unfavorable for induction, the patient was hospitalized until such a procedure became feasible, or until a spontaneous onset of labor ensued.

If, however, the pregnancy was complicated by toxemia, progressive retinopathy or other vascular abnormality; if the duration of the diabetes was more than fifteen years, or juvenile in origin, or if the fetus was estimated to be large, elective cesarean section was carried out at the end of the thirty-seventh week, or sooner in the presence of serious complications. Previous infant loss or other obstetric factors were also regarded as indicating the desirability of abdominal delivery. These rules were not rigidly adhered to but were generally followed.

As in the past, our pediatric consultants have treated the infants of diabetic mothers as if they were premature, regardless of birth weight.³

RESULTS

In reporting our observation, we have employed the nomenclature recommended by the World Health Organization. Thus a "viable" fetus or infant is one weighing over 400 gm. or one delivered at the twentieth week of gestation, or after. The delivery of a dead fetus falling into this category is classified as a "stillbirth."

During the six-year period covered in the study there were 18,972 deliveries of all mothers at The Johns Hopkins Hospital, giving an observed incidence of deliveries of diabetic patients of 0.51 per cent or five in a thousand. This incidence is higher than that reported in other large maternity hospitals.² As shown in table 1, ninety-five out of the ninety-seven infants delivered at the hospital weighed 1,000 gm. or more. Of these, seventy-nine survived. A perinatal mortality rate of 18.6 per cent was observed. This total was partially accounted for by twelve stillbirths, in ten of which the birth weight was over 1,000 gm. In addition, there were six neonatal deaths. The incidence of perinatal infant death was essentially the same in the white and Negro racial groups, being 20.0 and 17.5 per cent. This

TABLE 1

General data on deliveries of diabetic mothers at The Johns Hopkins Hospital, Jan. 1, 1953, through Dec. 31, 1958

	Number	Per cent
Women delivered	85	
Deliveries	97	
Infants 1,000 gm. and over	95	
Perinatal mortality, total	18	18.6
Perinatal mortality, over 1,000 gm.	16	16.8
All stillbirths	12	
Stillbirths over 1,000 gm.	10	
Neonatal deaths	6	
Surviving infants	79	
Twins	0	
Maternal deaths	0	

mortality rate of 18.6 per cent is identical with that observed in the infants produced in fifty-six pregnancies in which the medical and obstetrical management was similar.³

Data regarding toxemia are presented in tables 2, 3 and 4. A patient's disorder was classified as preeclampsia or hypertensive disease according to criteria set by the American Committee on Maternal Welfare.⁷ Preeclampsia, according to this classification, indicates the development after the twenty-fourth week of pregnancy of one or more of the following manifestations: a sys-

TABLE 2

Incidence of toxemia in ninety-seven pregnancies

	Pregnancies	
	Number	Per cent
Preeclampsia	17	17.5
Hypertension	22	22.7
Toxemia total	39	40.2

TABLE 3

Perinatal mortality and type of toxemia

	Pregnancies		Deaths	
	Number	Per cent	Number	Per cent
No toxemia	58	10	17.2	
Preeclampsia	17	2	11.8	
Hypertension	22	6	27.2	

TABLE 4

Toxemia and perinatal mortality correlated with White's classification of diabetes

Class	Total Pregnancies		Toxemic Pregnancies		Deaths	
	Num-ber	Per cent	Num-ber	Per cent	Num-ber	Per cent
A	5	5.2	1	20.0	0	0.0
B	54	55.7	20	37.1	9	16.6
C	21	21.7	7	33.3	4	19.0
D	14	14.4	9	64.3	3	21.4
E	1	1.0	0	0.0	1	100.0
F	2	2.1	2	100.0	1	50.0

tolic blood pressure of 140 mm. of mercury or more or a rise of 30 mm. or more above the usual level; a diastolic pressure of 90 mm. or more, or a rise of 15 mm. or more above the usual level; proteinuria of significant degree; or persistent edema of the hands or face. Hypertensive vascular disease was diagnosed in those women manifesting a systolic blood pressure of 140 mm. or more or a diastolic pressure of 90 mm. or more before the twenty-fourth week of gestation, usually persisting after delivery, unrelated to pregnancy, and demonstrated to be present in the nonpregnant state.

Preeclampsia or hypertensive disease was present in 40.2 per cent of the pregnancies. Hypertensive disease comprised more than half of the group; it was present in 22.7 per cent of the ninety-seven pregnancies. Perinatal loss was highest in this group with hypertension, being 27.2 per cent, compared with the rate of 11.8 per cent in the preeclamptic group. This finding suggests that hypertensive vascular disease is a very serious complication in these diabetic patients. The fact that preeclampsia occurs predominantly in relatively younger women⁸ in whom diabetes may have been present for a shorter period of time may contribute to its less frequent association with perinatal death. We cannot offer impressive evidence for this explanation, however, since in the present study there were fifteen patients with preeclampsia in one or two pregnancies whose mean age was 29.2 years whereas the mean age of twenty-two women with hypertensive disease was 31.9 years. It is interesting to note in table 3 that, whereas the perinatal loss in the pregnancies in the nontoxemic group was 17.2 per cent and closely approximated the over-all loss of 18.6 per cent, the perinatal loss in pregnancies complicated by preeclampsia was only 11.8 per cent. It must be recognized that some of these deviations may be due to chance, since the number of subjects in each group is small.

White's criteria⁹ for classification of the severity of diabetes were used in the analysis of our data presented in table 4. White's classification is as follows: Class A—Glucose tolerance test slightly abnormal, no insulin needed, little dietary regulation; Class B—Onset of diabetes after twenty years of age or diabetes of less than ten years' duration, cases free of vascular disease; Class C—duration of diabetes long, ten to nineteen years, onset of diabetes between ages ten to nineteen, minimal vascular disease, such as retinal arteriosclerosis or calcification of the vessels of the legs alone; Class D—prolonged duration of diabetes for twenty years or more, onset of diabetes before age ten, evidence of vascular disease such as retinopathy, transitory albuminuria, or

transitory hypertension; Class E—pelvic arteries calcified; and Class F—all patients with nephritis.

As can be seen from table 4, most cases fell in Classes B, C, and D, which collectively account for 91.8 per cent of the series. The majority (55.7 per cent) of the patients were classified as Class B, and manifested relatively few complications of diabetes. The infant mortality rate and the incidence of toxemia in all classes save A were elevated above the over-all average for the obstetrical clinic. No deaths occurred in the Class A group (five deliveries).

Of the fifty cesarean sections performed, in twenty-eight instances the patient had undergone a previous section (table 5). This is in sharp contrast to the finding in our previous study³ that only three out of forty-four sections were not primary.

It will be noted that in table 6 consideration has been limited to those cases in which a living fetus was present at thirty-seven weeks of gestation. In this category there was observed a practically identical incidence of fetal death whether the infant was delivered by section or by vagina—8.3 and 10.3 per cent respectively.

Viable infant losses are reviewed in table 7. There were nine deaths in utero before labor (50 per cent of the group), three cases of death in utero during labor and six neonatal deaths. It is of interest that of the nine infants dying before labor, seven were the infants of mothers in whom control of diabetes was poor. For statistical purposes, we consider these seven deaths preventable. Of the remaining deaths, one was associated with hypertensive vascular disease and another occurred after the mother developed mumps at twenty-eight weeks.

Of the fetal deaths during labor, one involved a very

TABLE 5
Perinatal mortality related to method of delivery

Method	Deliveries		Deaths	
	Number	Per cent	Number	Per cent
Cesarean section	50	51.5	6	12.0
Vaginal delivery	47	48.5	12	25.5

TABLE 6
Perinatal mortality in eighty-seven pregnancies in which fetal heart was heard at thirty-seven weeks of gestation related to method of delivery

Method	Deliveries		Deaths	
	Number	Per cent	Number	Per cent
Cesarean section	48	55.2	4	8.3
Vaginal delivery	39	44.8	4	10.3

TABLE 7
Viable infant losses

Patient	Date fetal heart ceased Week	Infant weight Grams	White class	Known duration diabetes Years	Maternal weight Pounds	Maximum dose insulin Units/day	Remarks*
A. Fetal death in utero before labor							
1	36	3,220	D	4	138	30	Hypertension
2	30	2,420	B	1	242	60	Poor regulation, hypertension
3	27	645	E	11	183	15	Poor regulation
4	33	2,350	B	1	152	150	Poor regulation
5	33	1,845	F	17	129	74	Poor regulation, hypertension
6	33	1,725	D	11	172	60	Poor regulation
7	37	3,650	B	0	266	0	No regulation (diagnosed post-partum), preeclampsia
8	32	630	C	12	147	50	Mumps at twenty-eight weeks, preeclampsia
9	37	1,550	B	4	193	0	Poor regulation
B. Fetal death in utero during labor							
10	39	4,250	B	1/12	187	0	Shoulder dystocia, poor regulation
11	39	5,600	B	2/12	300	15	Section, hysterectomy, hypertension, poor regulation
12	41	3,800	B	1/12	353	25	Extreme maternal obesity
C. Neonatal deaths							
13	33	2,410	D	12	150	80	Section, hypertension, diabetic retinopathy
14	39	1,700	B	3	264	30	Section, duration of pregnancy questionable, hypertension
15	31	1,920	C	13	170	0	Microcephaly
16	33	2,980	C	11	130	90	Section
17	37	2,945	C	11	147	60	Section, multiple fetal anomalies, poor regulation
18	37	3,930	B	2	215	20	Section, fetal renal arteries thrombosed

*Unless delivery by cesarean section ("section") is indicated, deliveries were vaginal.

TABLE 8
Perinatal mortality and infant weight

Weight Grams	Infants Number	Deaths	
		Number	Per cent
400-999	2	2	100.0
1,000-1,499	2	0	0.0
1,500-1,999	9	5	56.0
2,000-2,499	4	3	75.0
2,500-2,999	14	2	14.3
3,000-3,499	18	1	5.5
3,500-3,999	24	3	12.5
4,000-4,499	14	1	7.1
4,500-4,999	8	0	0.0
5,000-5,499	1	0	0.0
5,500 +	1	1	100.0

obese woman whose infant was injured during delivery; there was a question whether or not the fetal heart was heard on admission. A cesarean section and hysterectomy were performed. In another delivery complicated by shoulder dystocia, attempts at delivery before

admission to the hospital had fatally mutilated the infant. The third instance involved the infant of a tremendously obese woman who presented in labor after a forty-one-week gestation period. The second stage of her labor was very prolonged.

Of six neonatal deaths, five occurred in infants who had been delivered by cesarean section. This group included the two infants manifesting anatomical anomalies. There was a third infant with thrombosed renal arteries. Another neonatal death occurred after a mother was delivered at thirty-three weeks by cesarean section because of hypertensive vascular disease and diabetic retinopathy. Hyaline membrane disease was found at autopsy in the lungs of the other two infants. It is to be noted that in no infant which was delivered vaginally was a hyaline membrane found at autopsy, although one infant who survived was treated for this condition for several days because the diagnosis was suspected.

Infant mortality is correlated with birth weight in

table 8. The lowest mortality rate, 5.5 per cent, occurred in the group weighing 3,000 to 3,499 gm. with one death in eighteen deliveries. Closely similar to this rate were those of the groups weighing between 2,500 and 2,999 gm. and between 3,500 and 3,999 gm., 14.3 and 12.5 per cent respectively. Death occurred more frequently in infants weighing below 2,500 gm.; there were ten deaths in seventeen deliveries, a 59 per cent mortality rate.

DISCUSSION

Most of the mothers we are reporting upon were observed in the prenatal diabetes clinic, where patients are seen on a referral basis. No special efforts have been made to find "prediabetic" subjects or women with Class A diabetes among the patients presenting themselves to the general obstetrical clinic through the routine use of glucose tolerance tests. Wilkerson's studies,¹⁰ as yet incomplete, may demonstrate the desirability of such a procedure. We have performed glucose tolerance tests only in those patients in whom we suspected diabetes because of previous fetal losses, a family history of diabetes, previous large babies, or the presence or history of hydramnios, toxemia, or glycosuria. Therefore, the number of Class A diabetic patients in this series is less than that of other series now being reported.

Patients who were not followed in the prenatal diabetes clinic are included in the statistics. Seven fetal deaths occurred in utero in the infants of patients whose diabetes was poorly controlled (table 7). These patients represented some of those who either received no prenatal care, or those in whom habitual failure to follow instructions prevented reduction of hyperglycemia. These seven deaths are therefore considered preventable. When we consider this group in conjunction with the three deaths occurring during labor, we find that ten, or 55 per cent, of the deaths, were possibly preventable.

A problem found among patients who were followed in the clinic was inability or unwillingness of many patients to undergo hospitalization as often as was deemed necessary. This factor operated adversely, but the extent of its influence could not be estimated fully. Preeclamptic patients were admitted sooner and were treated more vigorously than those with hypertension. Their management included more sedation and earlier delivery.

Regarding the use of cesarean section, no hard and fast rules were followed. Each case was evaluated individually, consideration being given to all the variables involved. Inspection of tables 6 and 7 may lead to the conclusion that cesarean section was of no help or was even detrimental in some cases. It must not be forgotten,

however, that this operation was often performed under the circumstances of increased incidence of maternal vascular disease. Further, sections were carried out in many instances in patients whose complications, such as fetal-pelvic disproportion, were obstetrical, although produced by diabetes. Cesarean section continues to be of value in the presence of toxemia and other situations in which early termination of pregnancy is indicated.

The perinatal mortality rate of 18.6 per cent observed in these ninety-seven recent pregnancies is identical with the 18 per cent recorded by us for an earlier series of fifty-six diabetic pregnancies which were conducted in a similar manner.⁸ The only differences in the management of the two groups were that (a) relatively more patients were followed by local physicians in county clinics in the more recent period, (b) more emphasis was placed on restriction of the fat in the diet in the second series, and (c) more intermediate insulin (NPH or Lente) and less Protamine Zinc Insulin were used in the present series.

Various provocative reports on the outcome of diabetic pregnancies have been published describing considerable variations in fetal mortality.¹¹⁻¹⁵ These differences seem to depend on such factors as the number of Class A diabetic patients, the proportion of those with juvenile diabetes, the number of patients with inadequate prenatal care, the use of delivery employing induction and cesarean section and the number of those pregnancies excluded as "previable." Thus it often seems inappropriate to compare one series with another. The method of selection of the diabetic mother reported upon by Hagbard¹² was relatively similar to that we utilized, as were the clinical methods employed; differences included Hagbard's more frequent utilization of cesarean section at thirty-seven weeks of pregnancy and the physical dispersion of his observing clinics. Hagbard reported a total perinatal mortality of 26 per cent, with 14 per cent stillbirths and 12 per cent neonatal mortality.

It is clear that, given our incomplete knowledge of the cause of intrauterine death in diabetes, the rather simple educational background of a majority of our clinic population, and the late stage of pregnancy at which some of the subjects presented themselves for care, the technics we have employed do not prevent infant disaster in one of five pregnancies. This fetal wastage is approximately five times that recorded for all pregnancies at our hospital; it is, however, only half the fetal wastage (36 per cent) observed in our Obstetrical Clinic before the institution of a special service for diabetic mothers in 1948.⁸ Our same technics employed in the care of an educationally and economically

more privileged group could be expected to effect a reduction in fetal loss below 18 per cent on the assumption that more satisfactory regulation of diabetes, and hence fewer fetal deaths, will ensue in this setting.

In this regard, the tabulated data available to us do not permit an exact comparison of the relative excellence of control of the diabetes in the mothers producing infants which survived with the degree of control achieved in the mothers whose fetuses did not survive. A review of the information on our series which is at hand suggests a higher incidence of impressive hyperglycemia in the mothers in whom the pregnancy was unsuccessful. Thus, in ten out of eighteen mothers encountering an unsuccessful pregnancy the control of diabetes was grossly unsatisfactory.

During the course of our study, our interest was directed toward the subject of neonatal infant hypoglycemia. The incidence and interpretation of this phenomenon are widely debated by those concerned with the care of the infants of diabetic women. Many observers have denied its occurrence except as produced by mismanagement of insulin administration on the day of delivery. In this series of ninety-seven deliveries, the blood sugar of many of the infants was measured. Neonatal hypoglycemia with serum glucose less than 25 mg. per 100 ml. occurred in ten infants. A common factor was sought for but not found. Maternal insulin dosage varied from zero to 115 units. No patient had preeclampsia; one had essential hypertension. Nine of the ten patients were delivered by cesarean section while one delivered spontaneously. The diabetes of all patients was classified as Class B or C. We do not attempt to explain the fact that at least 10.3 per cent of our infants manifested this difficulty, but we do feel that insulin dosage and toxemia were not consistently significant factors.

SUMMARY

Ninety-seven viable pregnancies in eighty-five women manifesting diabetes mellitus were observed at The Johns Hopkins Hospital between Jan. 1, 1953, and Dec. 31, 1958. The observed incidence of diabetic deliveries during that period was five in 1,000 deliveries.

Measures employed in the management of the pregnancies included strict regulation of the diabetes; delivery when feasible at the end of the thirty-seventh week, by cesarean section in selected cases; and treatment of the infant as if he were born prematurely.

There were eighteen perinatal deaths, equivalent to an infant mortality rate of 18.6 per cent. This is identical with the rate we reported previously for a similarly treated series of fifty-six diabetic pregnancies.³ Seven of

the intrauterine deaths in the present series occurred in the infants of mothers whose diabetes was uncontrolled; another three deaths occurred during labor. These ten deaths, half of the total of eighteen, are considered preventable. No maternal deaths occurred.

It is felt that more frequent hospitalizations, sometimes for prolonged periods of time, would be of benefit in our particular clinic population.

In our small series long-standing hypertension was even more dangerous to the fetus than was preeclampsia.

Ten instances of neonatal fetal hypoglycemia, with blood sugars below 25 mg. per 100 ml., were observed in association with the deliveries. No suitable single explanation was found.

SUMMARIO IN INTERLINGUA

Diabete Mellite e Pregnantia. Nove Experimentias in le Combattimento de Perinatal Mortalitate Fetal

Novanta-septe viable pregnantias in octanta-cinque feminas con manifeste diabete mellite esseva observate al Hospital Johns Hopkins inter le 1 de januario 1953 e le 31 de decembre 1958. Le incidentia de parturitiones diabetic observate durante ille periodo esseva cinque in 1000.

Le mesuras empleate in le manipulation del pregnantias includeva un stricte regulation del diabete, effectuation—in tanto que possibile—del parturition al fin de trenta-septe septimanas de gestation (per section cesaree in seligite casos), e tractamento del infante como si ille esseva nato prematur.

Esseva contate dece-octo mortes perinatal, equivalente a un mortalitate infantil de 18,6 pro cento. Isto es identic con le incidentia previemente reportate per nos pro un similemente tractate serie de cinquanta-sex pregnantias diabetic. Septe del mortes intrauterin in le presente serie occurreva in le infantes de matres in qui le diabete non esseva stabilisate. Tres mortes additional occurreva durante le labores. Iste mortes—representante plus que un medietate del total de 18 mortes—es considerate como prevenibile. Nulle morte materne occurreva in le serie.

Es opiniate que plus frequente hospitalisationes—in certe casos pro prolongate periodos de tempore—esserea de beneficio in nostre typo de population clinic.

In le presente serie—que non esseva extense—hypertension de longe durantia esseva mesmo plus periculose pro le feto que preeclampsia.

Esseva observate dece casos de neonatal hypoglycemia fetal, con nivellos de sucro sanguinee de infra 25 mg per 100 ml al tempore del parturition. Nulle satisfacente explication de iste constatacion esseva trovate.

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Miss Ella Rowe, R.N., of the obstetrical outpatient nursing staff, rendered valuable assistance in the management of the patients reported upon in this study. Dr. Court held a Department of Medicine fellowship in the Private Patient Clinic during part of the period devoted to this study. Dr. Thaddeus E. Prout of the Department of Medicine reviewed an early stage of the manuscript.

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On Teaching Diabetes

Laboratory Work on Diabetes in the Basic Science Departments

A group of medical students may be given some hypophysectomized rats to follow for several weeks. The curves of these rats are compared with those of: (1) control rats subjected to sham operations and (2) hypophysectomized rats treated with growth hormone. After these animals have been observed for three weeks, an appropriate dose of insulin is injected in each. Then the student can see the marked hypersensitivity of hypophysectomized rats to insulin and can compare this reaction to that of normal animals and of animals treated with growth hormone. After these studies are completed, the animals can be killed and the histologic width of epiphyseal cartilage of each can be measured. In this way the respective effects on cartilage growth produced by hypophysectomy and by growth hormone can be estimated. Then, simply by weighing the other endocrine glands, the medical student can readily demonstrate that hypophysectomy produces marked atrophy of the adrenal, thyroid, and gonads, and that the weights of these glands are not restored by administering growth hormone. Similar experiments can be devised to show graphically the effects of the adrenotropic and gonadotropic hormones.

These and many similar experiments can be performed within the first year of the medical school cur-

riculum. Since they are somewhat more complex than the traditional experiments, the students must plan for them with special care. If, for example, they are to collect twenty-four-hour urine excretions over a two-to three-week period (including Saturdays and Sundays) and if they are to administer insulin at specified intervals, they must rearrange their schedules accordingly.

Setting up a group of experiments of the type outlined does not necessarily require an integrated teaching program. Even with a classical departmentalized approach one can use a portion of the laboratory time ordinarily allotted to teaching anatomy, physiology, biochemistry and set up a group of endocrine experiments toward the end of the freshman year of medical school. Since each student would be involved in one of a possible dozen endocrine experiments, it is desirable to have each group present the results of its particular experiment to the entire class, to discuss the scientific background of the experiment, and to answer the questions of their fellow students.

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