dazole. This same order of activity also exists for inhibition of heme synthesis from glycine by chicken erythrocytes(2,3). The correlation between effect upon heme synthesis and dye destruction, however, is not as good with some of the other benzimidazoles. Certain of the 5-nitro and 5-chloro derivatives are inhibitory in the erythrocyte system(14) while they had little effect upon azo dye destruction. Additional experiments are needed to determine whether anti-cancer properties may be correlated with inhibition of dye destruction or with inhibition in the chicken erythrocyte system. Studies on metabolism of azo dyes with relation to the genesis of liver neoplasia as yet have not revealed the mechanism of the process. Further studies of possible interrelationships between azo dye carcinogenesis, the mechanism of dye destruction in liver homogenates and glycine incorporation in nucleated erythrocytes, might provide some basic information.

Summary. Certain benzimidazole, benzothiazole, indole, and quinoline derivatives, and auramine, inhibit destruction of the azo dye, 4-dimethylaminoazobenzene, by liver homogenates. This inhibition can be partially overcome by addition of riboflavin adenine dinucleotide and to a lesser extent by riboflavin phosphate. Correlation of inhibition of *in vitro* dye destruction and of heme synthesis by avian erythrocytes with the anti-azo dye carcinogenic effect of certain benzimidazoles is discussed.

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Renal Function in Human Pregnancy. I. Changes in Glomerular Filtration Rate and Renal Plasma Flow* (23790)

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The reports on the effects of pregnancy on renal functions have been controversial. Earlier investigators(1,2,3) have asserted that pregnancy does not alter renal functions while more recent studies(4,5) have shown a progressive increase in renal plasma flow (RPF) and glomerular filtration rate (GFR) which reaches a maximum around the eighth month of gestation and returns to near normal non-pregnant values after gestation. This divergency of opinion is probably due to the fact that the data reported by various authors were obtained from different groups of patients studied at different periods of gestation and were compared to still another group of non-pregnant individuals.

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The present study was aimed at investigating renal plasma flow and glomerular filtration rate in the same individual at various periods of gestation and after delivery. In this way the subject serves as her own control and errors from patient variation are eliminated.

Material and methods. Nine patients with normal pregnancy and without any history of cardiovascular or renal disease were selected. Each patient was studied in the first trimester (12-15 weeks), 2nd trimester (22-28 weeks) and 3rd trimester (33-37 weeks) of pregnancy and 6 to 8 weeks after delivery. The studies were conducted in the post-absorptive state with the patient in the recumbent position. Water diuresis was induced by liberal use of oral fluids just before and during the renal test and by intravenous isotonic glucose solution. A priming dose of inulin and PAH, calculated for each patient according to body weight, was injected intravenously over a period of 2 to 3 minutes and was followed by a sustaining infusion aimed at maintaining plasma levels of 200 mg/l of inulin and 30 mg/l of PAH. An equilibration period of 30 to 45 minutes was allowed after which 4 to 6 clearances of 20 to 30 minutes duration were obtained. Completeness of urine collections was achieved by exerting suprapubic pressure and by injecting air into the bladder. Blood samples were obtained at the midpoint of each collection. Inulin and PAH in blood

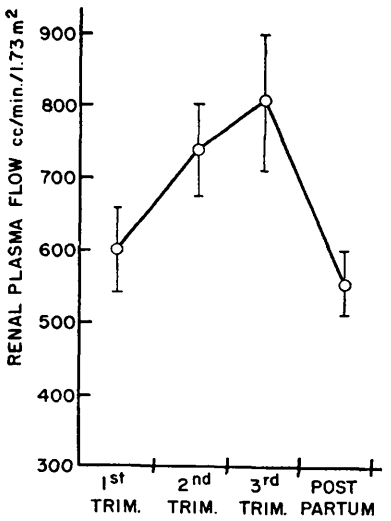

FIG. 1. Changes in renal plasma flow during normal pregnancy and after delivery.

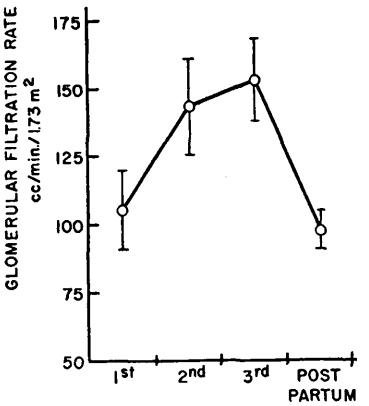

FIG. 2. Changes in glomerular filtration rate during normal pregnancy and after delivery.

and urine were analyzed by methods in current use in these laboratories. RPF was estimated from the PAH and GFR from the inulin clearances. It has been shown(4,6) that these substances are as suitable in the pregnant as in the non-pregnant subject to measure RPF and GFR.

Results. Fig. 1 shows average PAH clearances for the 9 patients during the 1st, 2nd, and 3rd trimester of pregnancy and in the postpartum period. The vertical bars represent standard deviation of the mean. Renal plasma flow rose in each patient from the first to the second trimester with a further but a less striking rise between the second and third trimester of pregnancy. In the postpartum period, renal plasma flow fell to values below those observed in the first trimester of pregnancy. Fig. 2 shows the values for the inulin clearances. The pattern of change was the same as that seen with PAH. Marked individual variations in the values for both PAH and inulin clearances occurred and were more evident during pregnancy than in the postpartum period.

Discussion. The present data are in agreement with those of Bonsnes and Lange(5) and Bucht(4) and show a significant rise in both renal plasma flow and glomerular filtration during pregnancy with a return to normal non-pregnant values 6 to 8 weeks after delivery. The rise was already evident in the 1st trimester but it was more striking during the 2nd and 3rd trimester of pregnancy.

There is a common belief among obstetri-

cians that the increased metabolic processes of pregnancy place a burden on the kidneys. The term "low reserve kidney" is frequently mentioned in obstetrics and usually denotes a kidney nearly exhausted by pregnancy. This concept has led many obstetricians to advise against pregnancy in the presence of any renal abnormality. In view of the increase in renal circulation and in glomerular filtration rate in pregnancy, this concept seems to be untenable.

Summary. 1. Renal function studies were performed on 9 patients during 1st. 2nd and 3rd trimester of pregnancy and in the postpartum period. 2. A progressive increase in renal plasma flow and glomerular filtration occurred, reaching maximum in 3rd trimester and returning to non-pregnant levels after delivery. 3. These changes speak against an added burden imposed on the kidneys by pregnancy.

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Effects of Superimposed Native Insulin on Disposal of Iodoinsulin in the Body.*† (23791)

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Iodoinsulin is widely used as a tracer in work designed to study the physiology of insulin. It is assumed that the iodinated compound is treated like native insulin by the tissues of the body. The validity of this assumption is supported by the observation that the breakdown of iodoinsulin in the body can be slowed by simultaneous administration of large doses of native insulin(1). This suggests the degrading processes of the two compounds are related and that some at least of the degrading mechanisms do not distinguish between them. Additional support for this assumption was given by our finding that biological activity resulting from a dose of native insulin decayed at the same rate as labeled insulin given at the same time to eviscerated-nephrectomized rabbits(2). In the intact animal the decay rate of iodoinsulin is very rapid. Greeley found the decay of biological activity to be much slower(3). There are many possible causes for this discrepancy. The kidney and liver, which actively degrade iodoinsulin, may treat native insulin differently. Another possible cause of the discrepancy is that iodoinsulin is ordinarily used in tracer amounts whereas appreciable dosages of insulin must be given to follow biological activity. Large doses of native insulin definitely lower the decay rate of iodoinsulin when the two are given together(1). It is possible that the smaller doses used to study biological activity could also produce such an effect. The experiments reported in this paper were planned to study this factor. The decay of iodoinsulin in the intact animal is so rapid that it would be difficult to detect small changes that might be effected by moderate doses of native insulin. Very large doses of

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