virus by inoculating mice intracranially with an approximate 10% suspension of the organs in 0.85%, NaCl solution. The presence of the characteristic clusters of elementary bodies in impression smears of the brain of mice dying 3 to 7 days after inoculation with the suspected material was taken as evidence of the presence of virus in the organ tested.

Birds inoculated intracranially died 3 to 15 days later and showed no gross abnormalities. Virus was present in the kidney and combined liver and spleen as well as in the brain.

In birds inoculated intraperitoneally the spleen was enlarged and soft, and the liver showed gross areas of focal necrosis, while the remaining organs appeared normal. Virus was recovered from the brain, kidney, and combined liver and spleen.

The oral-gastric route of infection was selected as approximating a natural mode of bird to bird transmission of virus. It was recovered from the organs of 7 of the 15 birds inoculated by this route which survived the first 7 days, and was present in the kidneys of 6 of these. Serum from 2 birds killed on the 14th day, from only one of which virus was recovered, fixed complement in the presence of psittacosis antigen, but serum from 2 others from which virus was recovered did not fix complement. Six other samples from uninfected birds were negative. The failure to demonstrate antibodies in birds from which virus is recovered may be due to a delay in antibody production as has been observed in pigeons.[6]

Summary. A serologically diagnosed case of psittacosis following exposure to a sick English sparrow and its droppings suggested an investigation of this species of bird as a carrier of psittacosis virus. 103 sparrows were examined for presence of active virus and serum from 59 of them were tested for complement fixing antibodies, but no evidence of natural infection was obtained. Four birds inoculated intracranially, 2 inoculated intraperitoneally and 7 of 15 inoculated by the oral-gastric route with psittacosis virus of pigeon origin became infected and virus was recovered from their organs.

[6] Meyer, K. F., Eddie, B., and Yanamura, H. Y., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 609.

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Tyrosine Tolerance Test in Pregnancy and the Puerperium.*

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We have shown previously that in normal pregnancy there is a marked increase in the excretion of both ingested and intravenously administered histidine, and that this is associated with a reduction of renal tubular reabsorption as well as with a delayed gastrointestinal absorption of this particular amino acid.[1,2] There is no apparent change, however, in the rate at which histidine disappears from the blood stream. The strange rejection of this important amino acid by both the renal and gastrointestinal epithelium during normal pregnancy is unexplained; we wished, therefore, to compare this finding with the metabolism and excretion of another amino acid, tyrosine, by the maternal organism. It would be desirable to know, furthermore, whether a tyrosine tolerance test might be of use as a measure of liver function in the toxemias of late pregnancy.

Following the oral ingestion of as much as

* Investigation aided by a grant from the John and Mary R. Markle Foundation, New York.

[1] Page, E. W., *West. J. Surg.*, 1943, **51**, 482.

[2] Page, E. W., *Am. J. Obstet. and Gynec.*, 1946, **51**, 553.

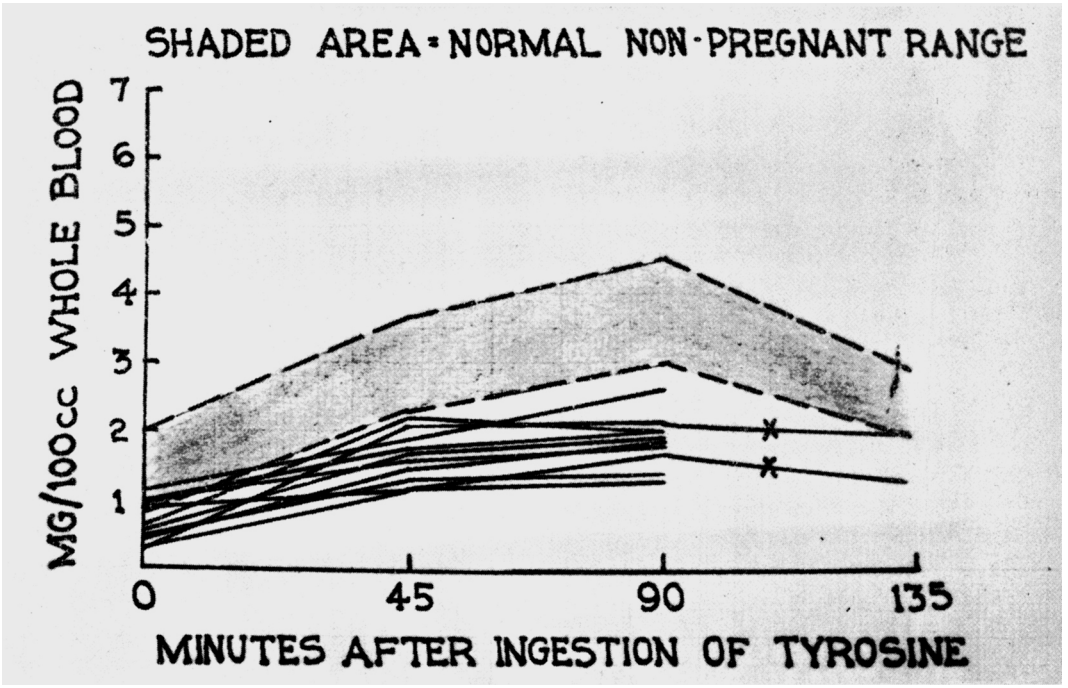

FIG. 1.
Tyrosine tolerance curves on 8 normal pregnant women and 2 women with severe toxemia (indicated by x). All values in 10 normal non-pregnant women fell within shaded area.

10 g of tyrosine by normal individuals, there are no significant changes in the urinary output of tyrosyl compounds.[3] The shape and height of the blood curve observed after such ingestion is therefore dependent upon two factors: the rate of absorption from the gastrointestinal tract and the rate of metabolism (utilization or destruction) of this compound. Bernhart and Schneider[4] followed the tyrosyl concentration of the blood at hourly intervals after the oral administration of 4 g of tyrosine, and suggested that this procedure be used as a test of liver function. The impaired metabolism of tyrosine associated with diseases of the liver results in a high initial level followed by an abnormal increase in the blood level at one hour and a delayed return to normal. In this respect, the type of curve obtained is analogous to the glucose tolerance curve associated with impaired carbohydrate metabolism. When there is delayed absorption from the gastrointestinal tract, on the other hand, as noted in patients with untreated pernicious anemia, the peak is simply delayed until about three hours after ingestion but is not abnormally elevated.[5]

Methods. Eight volunteer subjects with normal pregnancies of 7 to 9 months' duration, one patient with eclampsia and one with a severe grade of preeclampsia were selected for study. Seven additional women with normal pregnancies were studied from 1 to 36 hours after delivery. Ten control subjects of similar age were selected from preoperative patients on the gynecologic service. All of the latter group were in good general health with no history of liver disease. Each woman was fasting on the morning of the test, and was given 4 g of tyrosine in casein solution. The methods of analysis employed, based upon the Millon reaction, were identical with those of Bernhart and Schneider,[4] except that blood samples were taken at intervals of 45 minutes

[3] Medes, G., *Biochem. J.*, 1932, **26**, 917.

[4] Bernhart, F. W., and Schneider, R. W., *Am. J. Med. Sci.*, 1943, **205**, 636.

[5] Swenseid, M. E., and Bethell, F. H., *Proc. Centr. Soc. Clin. Res.*, 1944, **17**, 40.

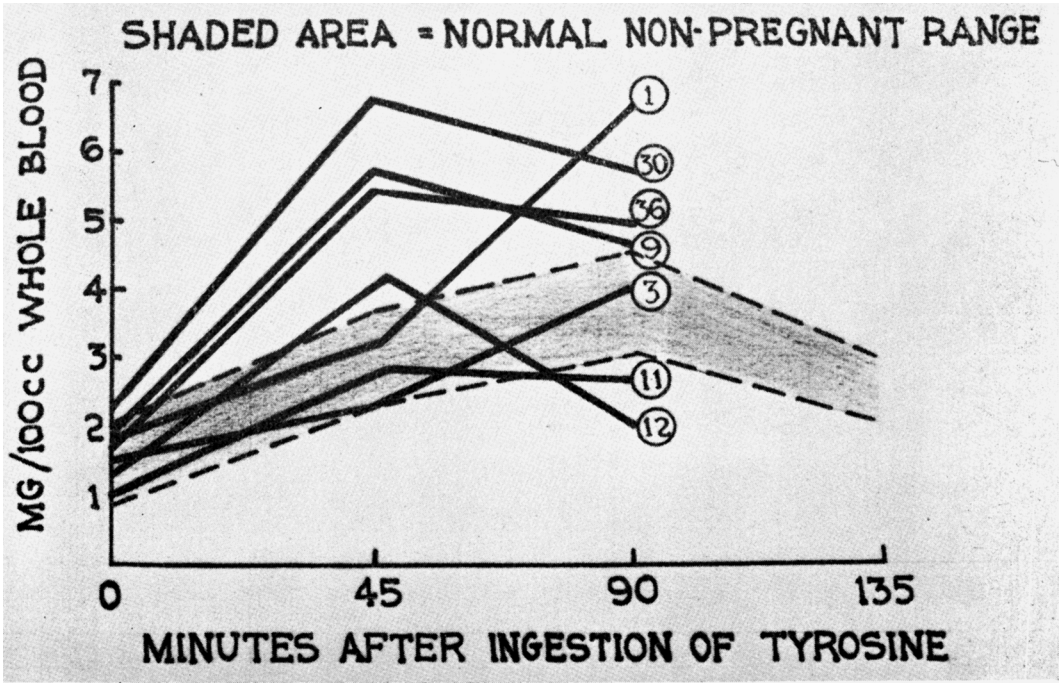

FIG. 2.
Tyrosine tolerance curves on 7 normal puerperal women. Figures in circle indicate the number of hours after delivery.

instead of hourly. This resulted in a change in the height and shape of the normal curve. In half the subjects of the normal non-pregnant and pregnant groups, urine samples were collected for a period of 8 hours before and 8 hours after administration of the tyrosine. These were analyzed for tyrosyl compounds by the Millon reaction as developed by Folin and Ciocalteu[6] and modified for urine determinations by Medes.[3]

Results. The fasting blood tyrosyl concentration of the 10 non-pregnant women was 1.44 mg/100 ml ± 0.09, with a standard deviation of 0.28. This compares favorably with the value of 1.4 as previously determined by the same method,[4] and with the value of 1.48 as determined by Hier and Bergheim[7] using microbiological methods. The fasting blood level of the 10 pregnant women was definitely lowered, being 0.99 mg/100 ml ± 0.12 with S.D. of 0.37. The difference between these means is 3 times the standard error of the difference and may be considered significant. On the other hand, the postpartum values were even higher than the non-pregnant level.

The tyrosine tolerance curves for the 8 normal pregnant women and the two toxemia cases are illustrated in Fig 1. It may be seen that the values remained low, but that the rate of rise is similar to that of normal non-pregnant women, though tending perhaps to be somewhat flatter. There was no apparent delay in gastro-intestinal absorption as described for cases of pernicious anemia. The average urinary output of tyrosyl compounds before the test was 147 mg/12 hrs, and this increased to an average of only 190 mg/12 hrs after the test. There were occasional falls rather than rises, and there were no discernible differences between the pregnant subjects, with or without toxemia, and the normal non-pregnant women.

Soon after delivery, however, there ap-

[6] Folin, O., and Ciocalteu, V., *J. Biol. Chem.*, 1927, **73**, 627.

[7] Hier, S. W., and Bergheim, O., *J. Biol. Chem.*, 1946, **163**, 129.

peared to be a shift in the metabolism of tyrosine. The type of curves (Fig. 2) suggest impaired liver function, but it is more likely that the shift represents a reduced rate of utilization of this amino acid for protein synthesis in contrast to an increased utilization prior to delivery. This is in keeping with the well-known transition from a positive to a negative nitrogen balance after delivery. In the two subjects tested only 1 and 3 hours post-partum, the blood values were still rising at 90 minutes, suggesting a delayed absorption. This may represent a persistence of the known delay in both stomach emptying time and absorption of foodstuffs during active labor. The fact that pregnancy and the puerperium alter the tyrosine tolerance curves in opposite directions from the normal, and the failure to find further alterations in the 2 severe toxemia cases, would make it hazardous to use this procedure as a liver function test in pregnant or puerperal women.

Conclusions. 1. The fasting blood tyrosyl level is significantly lowered during normal pregnancy, but not in the puerperium.

2. The reduced tyrosine tolerance curve during pregnancy suggests an increased rate of metabolism for this amino acid. There is an immediate reversal of this effect after delivery.

3. Unlike histidine, the renal tubular reabsorption of tyrosine appears to be as complete in pregnant as in non-pregnant subjects.

4. No alterations in tyrosine tolerance were noted in a case of preeclampsia nor in a case of eclampsia.

5. The observed shifts in tyrosine metabolism, possibly concerned with similar shifts in rates of protein synthesis, would probably invalidate the tyrosine tolerance test as a measure of liver function in pregnant and puerperal women.

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Further Studies on Renal Hyperlipemia.*

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Previous work[1,2,3] has shown that in dogs and rats unilateral and bilateral nephrectomy and the parenteral administration of nephrotoxic agents like mercury bichloride, uranium nitrate and potassium dichromate are followed by an increased blood lipid concentration. This effect of bilateral renal ablation has been confirmed by Winkler and associates[4] in dogs, has been recorded by these authors in monkeys, and by Nekludow[5] in cats. Hyperlipemia has also been found in rats made experimentally nephritic either by injection of antikidney serum[6] or by immunization with streptococcus—kidney antigen.[7] Hence, the kidneys of dogs, cats, rats and monkeys seem to function as part of a mechanism which influences blood lipid concentration.

Whether hyperlipemia also follows nephrectomy or renal injury in human beings has been investigated, and animal experiments have been carried out in an attempt

* Aided by a grant from the John and Mary R. Markle Foundation.

1 Heymann, W., *Science*, 1942, **96**, 163.

2 Heymann, W., and Clark, E. C., *Am. J. Dis. Child.*, 1945, **70**, 74.

3 Heymann, W., and Sekerak, B., PROC. SOC. EXP. BIOL. AND MED., 1945, **60**, 276.

4 Winkler, A. W., Durlacher, S. H., Hoff, H. E., and Mann, E. B., *J. Exp. Med.*, 1943, **77**, 473.

5 Nekludow, W. N., *Z. f. d. ges. exp. Med.*, 1925, **47**, 70.

6 Farr, L. E., Smadel, J. E., and Holden, R. F., Jr., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 178

7 Cavelti, P. A., and Cavelti, E. S., *Arch. Path.*, 1945, **40**, 163.