metabolized to known benzene metabolites (Parke & Williams, 1953*b*), mainly phenol, which is excreted in the urine as conjugates.

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The Effect of Testosterone on the Biliary Excretion of Tartrazine in Female Rats

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It has been shown that there is a sex difference in the extent of the biliary excretion of tartrazine in rats, the females excreting 2–3 times as much of the unchanged dye in the bile as the males. Tartrazine is not metabolized and is excreted unchanged in the bile and urine (Gregson *et al.*, 1972).

It has now been found that such a sex difference does not occur in guinea pigs (Duncan Hartley albino), both sexes excreting about 30–40% of an intravenously injected dose of the dye (50μmol/kg) in the bile in 3h.

The sex difference in rats (Wistar albino) has been further investigated. The renal pedicles of biliary cannulated male and female rats were ligated to prevent urinary excretion, and the extent of biliary elimination of intravenously injected tartrazine (50μmol/kg) was measured. Under these conditions the males excreted about 22% and the females 63% of the dose of tartrazine in the bile in 3h. This suggested that the sex difference in biliary excretion was not due to more rapid urinary excretion of the dye by the males, since in rats with functioning kidneys the values were 18 and 33% for males and females respectively.

Female rats were injected subcutaneously each day for 28 days with testosterone propionate (2.5 mg/kg per day) in arachis oil (0.5ml/kg) containing benzyl alcohol (10%, v/v). Control animals were injected daily with the same volume of the solvent only. On day 29 the rats were bile-duct-cannulated and the excretion of intravenously injected tartrazine (50μmol/kg) was measured. In the testosterone-treated females the biliary excretion in 3h was 14% (9–19%) and the urinary excretion 63% (55–70%) in eight animals. In eight control animals the biliary excretion was 31% (19–44%) and the urinary excretion 47% (41–53%). In normal male rats the corresponding values were 12 and 64% in 3h. Pretreatment with testosterone thus altered the extent of the biliary excretion of tartrazine in females to that of males.

The pretreatment with testosterone also altered the hexobarbitone sleeping times, for in the control female rats the sleeping time was 102min (91–138min) and in the treated females 57min (33–76min), the intraperitoneal dose of hexobarbitone being 100mg/kg. The hexobarbitone sleeping time for normal male rats was 23min (16–36min). Testosterone pretreatment of female rats therefore decreased the biliary excretion of tartrazine, which is not metabolized, and increased the rate of metabolism of hexobarbitone.

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Species Variations in the Metabolism of Phenol

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Marked species variations in the pattern of metabolism of a number of simple organic compounds, including benzoic acid (Bridges *et al.*, 1970), amphetamine (Dring *et al.*, 1970), phenylacetic acid (James *et al.*, 1971) and quinic acid (Adamson *et al.*, 1970), have been reported. These studies have now been extended to an examination of the species variation in the metabolism of [^{14}C]phenol in 19 species of animals. The animals were dosed orally or injected intraperitoneally with [^{14}C]phenol (25mg/kg), and urine was collected for 24h and then analysed for metabolites by paper chromatography followed by radiochromatogram scanning. For man (three male subjects) the oral dose was 0.01mg/kg and for the rhesus monkey it was 50mg/kg. The recovery of ^{14}C in the 24h urine ranged from 30% for the squirrel monkey to 95% for the rat; for most species it was about 50–70%.

Eight of the species examined, namely, the rat, mouse, jerboa, gerbil, hamster, lemming, guinea pig and man, excreted four metabolites, these being the sulphate and glucuronic acid conjugates of phenol and its oxidation product, quinol.