arsenic-o-aminoazotoluol treatment showed a proliferation of the bile ducts and a dense interstitial, round-cell infiltration (cirrhosis) of the liver, along with an adenomatoid hyperplasia of the liver cells in the central parts of the lobules. Neoplasms were not present in the rats. Heep suggested that the discrepancy between these results and those obtained by the Japanese workers might be due to differences in the vitamin content of the food given (diet of Heep for the rats was bread, turnips, and bacon). Kinosita and co-workers demonstrated later on that the oral feeding of butter yellow elicited hepatic cancers only in animals kept on the nutritionally deficient diet of unpolished rice, while such reactions did not occur in animals fed an adequate diet.

In spite of these negative results with o-aminoazotoluol, there can be no doubt about the hepato-carcinogenic action of this compound, as hepatomas could be produced with several derivatives of o-aminoazotoluol. Thus p-dimethylaminoazotoluol (butter-yellow) when added to their diet, causes carcinomas of the liver of cats (Kinosita). The neoplasms are mainly cholangiocarcinomas. P-dimethylaminoazotoluol is structurally isomeric with the carcinogenic o-aminoazotoluol as well as with the noncarcinogenic p-aminoazotoluol. Yoshida stated that diacetylaminoazotoluol acts like o-aminoazotoluol, but it acts more slowly and requires higher doses than o-aminoazotoluol for the production of hepatic neoplasia.

Some evidence has been advanced indicating that the chemical structure of these chemicals determines to a certain extent, the type of neoplastically reacting cells of the liver. Studying the effect of o-aminoazotoluol, dimethylaminoazobenzol, and a fat soluble fraction of tar, Hashida found that the toluol derivative stimulated the proliferation of bile ducts, while the tar fraction acted upon both cellular elements. A slight chemical modification in the composition or structure of the carcinogenic compounds changed their biological qualities fundamentally. P-aminoazobenzol and p-toluol-p-toluidine (p-aminoazotoluol) elicited hepatic degeneration, while diazoamino-o-benzol was inert (Nishiyama; and Yoshida). Yoshida noted that monoacetylaminoazotoluol and scarlet-red (diazotized aminoazotoluol coupled with beta-naphthol) were ineffective. This was confirmed by Brass, who injected rabbits with scarlet red oil for at least three and a half months after having previously produced a chronic arsenic poisoning in these animals. This investigator observed nodular hyperplasia of the liver with interstitial inflammation (cirrhosis of Laennec), which he attributed to the action of the aromatic amine.

Summarizing the various investigations on the carcinogenic action on the liver of azo and related compounds, Kinosita (1940) recorded the following results: Dimethylaminoazobenzene is strongly carcinogenic, while o-aminoazotoluene is less so; scarlet red and to a lesser degree sudan III, sudan II, toluneazonaphthol, sudan I, and Bordeaux red produce liver adenomas when fed to rats; 4′ oxalylamino 2:3′ dimethylazobenzene and 4′-succinylamino 2:3′ dimethylazobenzene are hepato-carcinogenic in rats; 4:4 tetramethyl-