injected subcutaneously (Yoshida). Nishiyama fed o-aminoazotoluol to mice and found in 6 out of 46 mice thus treated and surviving for more than 11 months, multiple hepato-carcinomas. One animal had, in addition to the hepatoma, a hemangioendothelioma of the liver. A second mouse showed a pulmonary neoplasm. There was hyperplasia of the bile ducts but no neoplastic proliferation of these elements. Shear repeated this experiment, but administered the chemical by repeated, subcutaneous injection into the axillary region (6 times during one year). The first hepatic tumor appeared after 11 months and was single. Liver tumors appearing subsequently were multiple. While tumor formation was not observed at the site of injection, an adenocarcinoma of the colon occurred in one of the mice.

A hetero-organic multiplicity of neoplastic responses to the administration of o-aminoazotoluol was observed by Yoshida, who recorded the occurrence of papillomas of the forestomach and of the urinary bladder in rats besides that of hepatic tumors. Apart from the multicentric genesis of the hepatic, neoplastic reactions of both the liver-cell and bile-duct types, there were frequently hepatic and bile-duct carcinomas in the same liver. The minimal exposure time, by feeding o-aminoazotoluol, was 135 days for rats, according to Yoshida. If the treatment was then discontinued, first adenomas and then carcinomas of the liver (195 days) were formed. The majority of carcinomas increased with the duration of the feeding time and finally reached 100 per cent of the rats treated for more than 250 days. The cancers which arose, after the treatment had been discontinued, seemed to be more malignant than those appearing during the time of treatment. Metastases of the liver tumors were found in the lungs and elsewhere.

Miura and Nishiyama reported separately the production of carcinomas of the liver in guinea pigs fed with unpolished rice and o-aminoazotoluol. Nishiyama noted, moreover, a squamous-cell metaplasia of the thyroid. Leghorn chickens fed or repeatedly injected intramuscularly with o-aminoazotoluol developed, in three instances, adenocarcinomas of the liver after an inflammatory degeneration of the liver cells and proliferation of the bile ducts (Aoji).

While these investigations seem to demonstrate rather definitely the hepatocarcinogenic action of o-aminoazotoluol, subsequent observations suggest that there may exist species specific differences in the neoplastic reactivity to this chemical. Such a response may depend, also, upon dietary factors influencing the hepatic metabolism and, thereby, the chemical character of the conversion products of o-aminoazotoluol in the liver. Yoshida reported that rabbits fed with o-aminoazotoluol developed a cirrhosis of the liver with nodular, regenerative hyperplasias of the liver cells; there was no cancerous reaction.

Heep treated rabbits and guinea pigs for four months with arsenic, preliminary to the administration of o-aminoazotoluol in the food. After 18 months of treatment with o-aminoazotoluol, the rabbits were without any pathological lesions in the liver. Rats subjected to the same type of combined