Carcinomas of the liver were present in all 23 male rats ingesting 4'-F-4-BAA; whereas, the 25 male rats given 4'-F-4-BAA and MCA did not have hepatic lesions. Metastases to the lungs were present in 4 rats with hepatic carcinomas. Not only did the rats in the group given the two chemicals not develop hepatic carcinomas, but they also did not develop hyperplastic nodules, i.e., precursors of carcinomas. The histopathology of hyperplastic nodules and carcinomas of the liver has been described in detail previously[8].

Three of 23 rats given 4'-F-4-BAA in the diet also had primary renal carcinomas and 2 had hyperplastic nodules, which precede the development of renal carcinomas. Renal lesions were not present in animals ingesting both chemicals. The histopathology has been described elsewhere[9].

Discussion. MCA decreases the incidence of carcinomas of the liver in rats given 3'-methyl-4-dimethylaminoazobenzene (3'-Me-DAB)[10]. The chemical protects against hepatic carcinogenesis and cirrhosis in rats ingesting 2-FAA or N-2-fluorenyldiacetamide[7,11]. The incidence of carcinomas of the liver is markedly reduced in rats given MCA and diethylnitrosamine simultaneously; however, it is only slightly decreased in rats receiving MCA and dimethylnitrosamine[12]. MCA also protects against hepatic carcinogenesis induced by 4'-F-4-BAA.

The mechanism by which MCA protects against hepatic carcinogenesis induced by 3'-Me-DAB or 2-FAA has been studied. MCA increases the activity of the enzymes concerned with the hydroxylation of aromatic amines and the reduction of azo bond linkage and the N-demethylation of amino azo dyes[13,14]. Presumably, MCA also increases the activity of the enzymes that hydroxylate 4'-F-4-BAA.

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Decreased Incidence of Renal Cell Carcinoma in Rats with One Kidney Ingesting N-4-(4'-Fluorobiphenyl)acetamide

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Summary. Buffalo strain male rats, 12 weeks of age, ingesting 0.04% N-4-(4'-fluorobiphenyl)acetamide in a semisynthetic diet with both kidneys intact were more susceptible to the development of hyperplasia and carcinomas of the kidney than were rats with a uninephrectomy.

The fluorinated biphenyl derivative of 2-acetylaminofluorene, N-4-(4'-fluorobiphenyl)acetamide (4'-F-4BAA), induces carcinomas of the kidney in rats[1–7]. Male rats are more susceptible to renal carcinogenesis than female rats and older rats are more susceptible than younger rats[8,9].

Since 4'-F-4BAA is not absorbed well from the gastrointestinal tract, much of the chemical remains in the feces of rats ingesting the diet[10]. It was felt that if the amount of target tissue, i.e. kidney, for the chemical to interact with was decreased, the incidence of carcinomas might be increased. Therefore, the incidence of renal lesions in intact animals ingesting 4'-F-4BAA was compared with that in animals with a uninephrectomy.

Methods. Inbred Buffalo strain male rats 12 weeks of age and weighing 266 to 281 g were used. There were 2 experimental groups of 20 rats each. The groups consisted of 1. intact male rats and 2. male rats with a left nephrectomy. Nephrectomies were performed 1 week before the start of the experiment.

The carcinogen was fed in Morris Diet No. 272[8]. 4'-F-4BAA was added in the amount of 0.04%. The carcinogen-containing diet was fed ad libitum continuously for 36 weeks. Thereafter, the rats were given Purina laboratory pellets. Animals were weighed every 2 weeks. 48 weeks after the start of the experiment all surviving animals were killed by exsanguination.

Complete necropsies were done at the time of death or killing of the animals. Tissues were fixed in 4% formaldehyde and stained routinely with hematoxylin and eosin, and when indicated, with the periodic acid-Schiff (PAS) technique.

The findings in the kidneys were classified as 1. no hyperplasia, 2. hyperplasia, 3. hyperplastic nodules, 4. small carcinomas (5 mm or less), and 5. large carcinomas (greater than 5 mm)[11].

Results. Animals of both groups steadily gained weight for 36 weeks, at which time the weights remained constant. Rats with a left nephrectomy survived for an average of 44 weeks (42 to 48); intact rats survived for 48 weeks. The number of animals with lesions of the kidney is shown in the Figure.

Carcinomas of the kidney were observed in 9 of 16 intact male rats; whereas 3 of 17 rats with the left kidney removed had renal cell carcinomas. The carcinomas in animals of the latter group were 5 mm or less in size. Hyperplastic renal nodules were present in 6 intact rats

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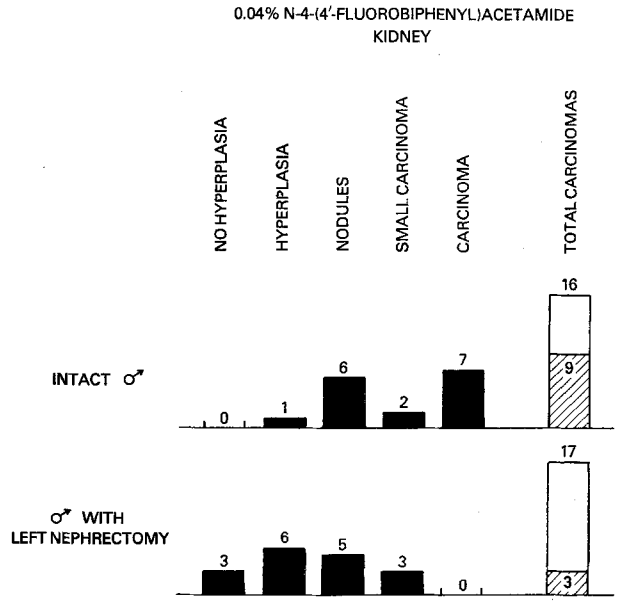
and 5 rats with a uninephrectomy that did not have carcinomas of the kidney.

Seven of 16 intact rats also developed carcinomas of the liver; however, the rats with renal carcinomas either did not have hepatic carcinomas or the carcinomas were less than 5 mm in size. The incidence of carcinomas of the liver was greater in the rats with a uninephrectomy (13 of 17) and the carcinomas were large[12].



The most advanced lesion in a given animal is indicated. Number above each black bar is the total number of animals developing such lesions. 'Total carcinomas' indicates total number of animals in the group, with the shaded area representing the number with carcinomas.

Discussion. Buffalo strain inbred male rats are more susceptible to hyperplasia and carcinomas of the kidney induced by 4'-F-4BAA[8,9]. Other studies concerning the influence of endogenous or exogenous factors on these renal lesions have not been done.

Renal tumors that occur in the intact male golden hamster given s.c. stilbestrol are inhibited by androgen[13]. Stilbestrol-treated hamsters with a uninephrectomy develop renal tumors much earlier than the treated intact animals[14]. It was postulated that stilbestrol may not be metabolized by the liver of the hamster, thus accounting for the fact that the hamster, and not other species, have stilbestrol-induced renal tumors.

4'-F-4BAA is metabolized by the rat liver and the metabolites are excreted by the kidneys. Animals with one kidney apparently were not able to secrete the metabolites of 4'-F-4BAA as readily as rats with both kidneys intact. The metabolites were returned to and acted upon the liver and increased the incidence of hepatic carcinomas[15].

It is not known whether4'-F- 4BAA or some metabolite causes carcinoma of the kidney or why there was a decreased incidence of renal carcinomas in rats with a unilateral nephrectomy.

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Uptake of L-Glutamate and L-Aspartate in Neurones and Glial Cells of Cultured Human and Rat Spinal Cord

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Summary. Autoradiographic investigations on the uptake of L-glutamate and L-aspartate have shown that the amino acids were taken up by neurones as well as by glial cells of cultured human and rat spinal cord. The activity of glutamate and aspartate varied considerably between individual neurones, whereas glial cells showed a more even distribution of the labelled amino acids. Our results suggest that both neurones and glial cells are involved in the uptake of amino acid transmitters.

Investigations on the regional distribution of L-glutamate and L-aspartate in the cat spinal cord have shown that the glutamate concentrations were highest in the dorsal grey and in the proximal part of the dorsal roots whereas aspartate levels were highest in the ventral grey[1-3]. It has been observed by electrophysiological studies that glutamate and aspartate depolarize spinal neurones (for ref. see[4]) and that this depolarization is associated with an increase in sodium permeability[5-7]. From these results it has been suggested that both amino acids may function as excitatory transmitters in the spinal cord, glutamate being released by primary afferent fibres[1,2,8] and aspartate being associated with interneurones[2].

It has been proposed that uptake may be an important mechanism for terminating the action of transmitter

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