Frequency of mouse jumping elicited by apomorphine

Drug	Dose (mg/kg)*	Mean mouse jumps**
Saline		1 (25)
Apomorphine	0.4	0 (8)
	1.0	0 (8)
	5.0	0 (8)
	7.5	0 (8)
	10.0	0 (8)
	25.0	0 (6)
	50.0	0 (4)

* Observation period was dose-dependent. See methods. ** Parenthesized numbers indicate mouse population size.

has been postulated[6] to have both direct and indirect agonist actions on both dopamine (DA) and norepinephrine (NE) activated neurons. Exogenous L-DOPA is not only converted to catecholamines in DA and NE neurons[6], but it is also taken up by serotonin neurons[7] and exerts an influence on various behaviors due to increased functional activity at serotonin synapses[8]. The importance of noradrenergic systems in jumping behavior has not been eliminated since the NE blocker tested, phentolamine, passes only poorly into the brain and causes few of the biochemical and functional changes seen with centrally active adrenergic blocking agents[9]. A further difficulty with the jumping behavior model is the inability of either amphetamine or L-DOPA alone to induce jumping[4].

The inhibition of L-DOPA and amphetamine induced jumping by neuroleptics and the reversal of this inhibition by anticholinergic agents has been cited[3] as evidence for the specific mediation of jumping behavior by DA systems. Many behavioral effects of neuroleptics are reversed in this manner[3], but the only area where biochemical antagonism has been well established is the Corpus Striatum[10]. If striatal DA systems were mediating jumping behavior, apomorphine, a potent DA agonist at this site, should also elicit jumping. It is possible that the inhibition of jumping by neuroleptics is a nonspecific antagonism secondary to the induction of catalepsy, which effect is elicited with relatively low doses of potent neuroleptics[11,12] and reversed by anticholinergic drugs[12,13].

In light of the multiple sites for activity and actions of the agonist drugs used in previous reports, and particularly in consideration of the results presented here, the proposal that jumping behavior induced by L-DOPA and amphetamine is specifically due to dopaminergic stimulation must be questioned. Finally, drugs such as narcotic antagonists, 5(1,3-dimethylbutyl)-5-ethylbarbituric acid, naphthyloxyacetic acid and theophylline have all been reported to induce mouse jumping[4], making a precise mechanism for jumping behavior very difficult to determine. Thus, with the availability of well established and pharmacologically specific models for dopaminergic stimulation[1,2], the value of employing jumping behavior for this purpose is limited.

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Retrograde lymphatic spread of colonic carcinoma to the liver

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Summary. Retrograde lymphatic permeation of the liver by a malignant neoplasm is an unusual phenomenon and has apparently not been reported with colonic carcinoma. This paper presents such a case; the features of the lesion are similar to those described for other primary sites.

Nonmetastatic invasion of the liver via lymphatic vessels is unusual[2-4]. Retrograde lymphatic permeation has been reported most frequently with gastric carcinoma; it also occurs with carcinoma of the pancreas, ovary, and cervix uteri[2,4]. Tumour deposits occur typically in the region of the porta hepatis and its lymph nodes, with extensions into the liver along the major portal tracts[5]. 'In this way, there may be formed a branching frond-like tumour mass, most bulky at the porta and becoming gradually attenuated peripherally, its ramifications corresponding to those of the portal tracts which the tumour thus delineates in grotesque fashion'[4]. Retrograde lymphatic spread does not seem to have been reported for colonic carcinoma, and has not been observed by R.A. Willis (personal communication).

Clinical summary. A 63-year-old man underwent right-sided hemicolectomy for a moderately differentiated adenocarcinoma of the caecum. 3 months later, multiple metastatic nodules were found in the abdominal wall and mesentery. He died 1 month later.

Autopsy findings. Cardiovascular system: thrombosis of the right external iliac, femoral, popliteal and deep calf veins. Respiratory system: bullous emphysema. Embolism of the left apical branch of the pulmonary artery. Infarction of the left apical segment, with infection and abscess formation. Alimentary system: faecal peritonitis. The site of leakage could not be identified. There was evidence of a previous Billroth II gastrectomy. The small intestine was distended and congested; numerous fibrinous adhesions were present. The carcinoma had recurred at the site of previous anastomosis. However, the anastomotic region was not fixed to adjacent structures and there was no evidence of contiguous spread of the tumour.

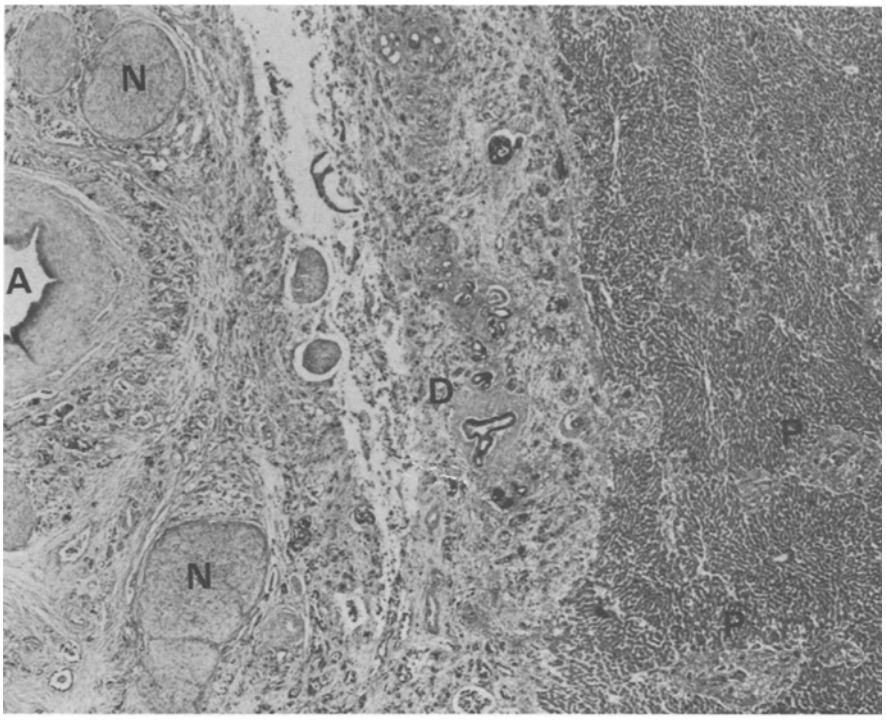

Fig. 1. Low-power micrograph of the liver illustrating a major neurovascular-ductal bundle and adjacent hepatic parenchyma. There is carcinomatous infiltration around the artery (A), peripheral nerves (N), bile ductule (D) and of the portal tracts (P). H & E ×22.

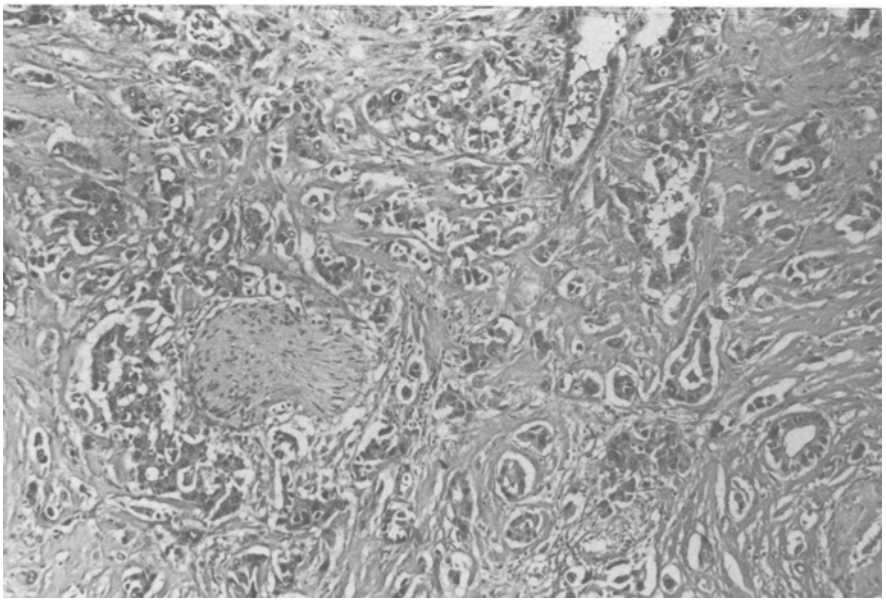

Fig. 2. Higher magnification from the area of neoplastic infiltration, showing a moderately differentiated adenocarcinoma surrounding a nerve bundle. H & E ×90.

The liver contained no metastatic nodules. However, the carcinoma had spread along the neurovascular-ductal bundles arising from the porta hepatis and formed a cuff of tumour tissue around the vessels, following them as they divided. The tumour involved lymph nodes in the porta hepatis.

Microscopic examination revealed a moderately differentiated adenocarcinoma that had infiltrated the submucosal, muscular and serosal layers of the intestine at the anastomotic sites. In the liver, there was extensive malignant infiltration of the major portal tracts, which also contained aggregates of chronic inflammatory cells. However, the zone of neoplastic infiltration was sharply demarcated from the hepatic parenchyma (figures 1 and 2).

This case therefore illustrates the typical features of retrograde lymphatic permeation of the liver by a malignant tumour, in this instance, a colonic carcinoma.

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