Alcohol and the Gastrointestinal Tract

NEVILLE KRASNER, MD, MRCP(UK)

Gastroenterologist, Royal Infirmary, Glasgow

The ambivalent attitude towards the consumption of alcohol is engendered by its accepted value as a social lubricant, on the one hand, and even sometimes as a source of calories, and, on the other, by the dangers that attend its misuse. It is hardly surprising that the gastrointestinal tract should be the site of a variety of toxic effects related to alcohol, since this is where absorption and the subsequent metabolism of the drug take place.

MOUTH AND OESOPHAGUS

In its rapid passage to the stomach, alcohol has little chance of damaging the mucosa of the mouth and oesophagus. Nevertheless, disease of the parotid gland is not uncommon in patients with alcohol-associated liver disease, and malnourished subjects deficient in iron and vitamin B complex may develop stomatitis and cheilitis. There is also the recorded association between heavy drinking and oesophageal carcinoma (McGlashan, 1969; Collis et al., 1972). Alcohol could be the major aetiological determinant, but concomitant heavy tobacco consumption (Schoenberg et al., 1971) and malnutrition might also be factors (Mowat and Brunt, 1976). Peripheral neuropathy is a frequent disturbance in chronic alcoholics and may cause disordered oesophageal motility (Winship et al., 1968). Finally, oesophageal varices due to alcoholic cirrhosis of the liver are too well-known for comment.

STOMACH

Ancient records refer to gastric disturbances related to alcoholic excess but authoritative praise of alcohol may also have contributed to the development of these disturbances. Beaumont in 1833, with his classic observations on Alexis St Martin, was probably the first to demonstrate the direct toxicity of alcohol to the gastric mucosa. More recently, fibreoptic endoscopy has made visible the acute superficial erosions that develop in the gastric mucosa after drinking bouts; these erosions may be associated with heavy bleeding. Both aspirin and alcohol induce changes in the permeability of the gastric mucosa to hydrogen ions, and disrupt the integrity of the gastric mucosal barrier (Davenport, 1969; Dinoso et al., 1970; Smith et al., 1971), and acute haemorrhagic gastritis is often found when there has been concomitant aspirin ingestion (Needham et al., 1971; Johnston et al.,...
The mucosa may be further damaged by the alteration in mucosal blood flow in response to alcohol (Augur, 1970). The relevance of changes in gastrin secretion is uncertain but they would probably be associated with changes in gastric acid secretion (Treffot, 1975).

Croft et al. (1966) have shown that patients with simple atrophic gastritis exhibit a high exfoliation rate of gastric epithelial cells. Similar studies have shown the effects of acute and long-term heavy ingestion of alcohol on the gastric mucosa (Krasner et al., 1974). A significant increase in cell exfoliation rate (CER) was found in subjects studied within 48 hours of a heavy drinking spree, but not in chronic excessive drinkers who had been in hospital for a week before measurement of the cell turnover was made. The increase in CER seems therefore to reflect the direct toxicity of alcohol on the gastric mucosa, and may provide part of the explanation for the development of acute gastric erosions and bleeding shortly after heavy drinking.

Gastric acid secretion following pentagastrin (Peptavlon) stimulation was studied in acute and chronic drinkers and the results were compared with values in patients with gastric or duodenal ulceration (Krasner, 1975). Alcoholics with duodenal ulcers showed a significantly higher acid output than chronic drinkers with no peptic ulceration and, in fact, the figures were similar for patients with duodenal ulcers, whether or not they were heavy drinkers. The results obtained in the non-ulcer alcoholic group were similar to those obtained in the non-drinking gastric ulcer subjects. Thus, although acid output in heavy drinkers without ulceration was not significantly lower than in normal healthy subjects, there was a definite trend towards a reduced secretion of gastric acid in chronic excessive drinkers. In contrast, recent drinking sprees produced no predictable alteration in stimulated acid secretion.

Several other studies have shown alterations in acid production in chronic heavy drinkers (Woodward et al., 1957; Small et al., 1959; Roberts, 1972). The variability of results reported is probably due to a combination of the duration of alcohol consumption and the quantity and type of alcohol consumed (Lawrence, 1966). An additional factor is the presence or absence of gastric atrophy. Atrophy reduces acid output whereas (histological) gastritis without atrophy may have no such effect. There is still considerable controversy over the ability of alcohol to induce chronic gastritis (Roberts, 1972; Whitehead, 1973; Joske et al., 1975; Williams, 1956; Woolf, 1970; Varis, 1971). In a study on gastric morphology, the prevalence of gastritis in acute bout drinkers was found to be similar to that in a control group of subjects with X-ray negative dyspepsia; however, chronic gastritis was found significantly more frequently in groups of chronic drinkers than in controls (Krasner, 1975). Dyspepsia is common in heavy drinking subjects, but there is no evidence that it is related to histological gastritis. Without doubt, however, disturbances of gastric function and morphology induced by alcohol contribute to the poor nutritional status of many heavy drinkers.
Several abnormalities of small intestinal absorption have been observed in chronic excessive drinkers (Small et al., 1959; Mezey et al., 1970; Israel et al., 1968). Subclinical protein malnutrition has been implicated as a major cause of malabsorption in alcoholics (Mezey et al., 1970), but alcohol itself probably exerts a direct toxic effect (Israel et al., 1969). In animal studies Baraona et al. (1974) have demonstrated that haemorrhagic erosions appear at the tips of intestinal villi after the acute administration of alcohol, and ultra-structural changes in small intestinal mucosa have been observed in response to alcohol (Rubin et al., 1972). Immediately after the ingestion of alcohol there is a high concentration in the jejunum, but within two hours jejunal levels are in equilibrium with the vascular space. Luminal concentrations of about 2 per cent are often found in the jejunum even after moderate alcohol consumption (Halstead et al., 1973). In a recent study on chronic alcoholic subjects (Krasner et al., 1976a) the findings of low blood levels of folic acid and ascorbic acid in 50 per cent of patients, and abnormal D-xylose absorption and faecal fat excretion in 30 per cent were in keeping with previous studies on heavy drinkers (Halstead et al., 1967; O'Keane et al., 1972; Small et al., 1959, Mezey et al., 1970). None of these individuals showed morphological changes in the jejunal mucosa on light microscopy and, while nutritional deficiency may, in fact, account for the reduced vitamin levels, malabsorption from the small bowel seems a more likely cause.

The absorptive capacity of the jejunum in alcoholism has been investigated using the triple lumen tube perfusion system developed by Russell et al. (1972). A highly significant reduction in sodium and chloride ions and water was seen in the alcoholic subjects when compared with values in healthy control individuals (Krasner et al., 1976a); there was a net secretion of water and electrolytes into the jejunum. Thus, it seems that chronic alcohol ingestion may contribute to nutritional deprivation by impairing the absorption of water-soluble nutrients. Folate deficiency per se has been shown to contribute to the development of malabsorption in alcoholics (Halstead et al., 1973b), but this type of malabsorption can be totally corrected by the administration of folate.

Absorption of electrolytes from the intestinal lumen mainly involves the process of active transport. Energy for cellular metabolism is derived from the splitting of the high energy phosphate bond of adenosine triphosphate (ATP) by the enzyme adenosine triphosphatase (ATPase). Alcohol has been shown to affect the ATP content and ATPase activity in several tissues (Israel et al., 1965; Walker and Gordon, 1970), and therefore it is possible that disturbance of water and electrolyte transport in the jejunum is caused by a direct enterotoxic effect of alcohol on this energy system. In vitro studies on isolated segments of guinea-pig jejunum exposed for one hour to 2 per cent ethanol showed that a significant reduction occurred in ATP concentration when compared with values in control
segments perfused with Krebs solution (Krasner et al., 1976b). No significant change was found in ATPase activities. In a further long-term experiment on rats fed 50 per cent alcohol intragastrically for two weeks, ATP and ATPase levels were measured after 24 hours without alcohol administration so that the acute effects of alcohol on the gut could subside (Krasner et al., 1976b); no significant alterations were noted in either ATP concentrations or ATPase activities. Thus, it appears that acute exposure of the jejunum to alcohol interferes with the process of active absorption of electrolytes and so also passively impairs the absorption of water. This impairment of water absorption may be partly responsible for the occurrence of diarrhoea after alcohol ingestion. Although the absorptive capacity of the small bowel may be impaired directly after drinking, these studies provide no evidence of prolonged alcoholic excess causing similar disturbances, and it is possible that in this situation nutritional deficiency caused by inadequate intake is of greater significance. It is worth while noting the evidence that prolonged alcohol ingestion may interfere with ileal function, and Lindenbaum and Lieber (1969) have observed an impairment of the absorption of vitamin B12 from the ileum.

**DIARRHOEA**

Diarrhoea is a symptom that relates to several areas of the gastrointestinal tract. Disease of the pancreas due to alcohol is one cause of diarrhoea and, in our clinic, steatorrhoea is a not uncommon presenting symptom in heavy-drinking patients. In patients with cholestatic jaundice related to alcohol abuse, diarrhoea and steatorrhoea are common problems and malabsorption of fat-soluble substances is found to a varying degree. Allied to this is the problem of disturbances of bile acid metabolism in patients with alcoholic liver disease and, in particular, in those with cirrhosis (Vlahcevic et al., 1972; Yoshida et al., 1975). In these subjects cholereic diarrhoea may occur. Impaired absorption, and even secretion of water into the intestinal lumen, after recent heavy drinking, has already been discussed (Krasner et al., 1976a) and may result in excessively fluid faeces. Finally, there is the possibility that a disturbance in the bacterial flora present in the gut after prolonged alcohol ingestion could be a cause of diarrhoea, but there is little direct evidence to support this theory.

**CONCLUSIONS**

That alcohol causes many functional and morphological disturbances in the gastrointestinal tract is beyond question. However, it is often difficult to determine the significance of individual toxic effects. Fortunately, many toxic effects relate to a recent bout of heavy drinking and, if the patient can be persuaded to curtail his alcohol consumption, normal function may be restored to the affected organs. By far the most serious problem is the dependent drinker whose prolonged alcohol consumption produces cumulative disorders of the
gastrointestinal tract, which, combined with a totally inadequate food intake, inevitably lead to profound nutritional deprivation.

This article is based on a paper read at the Fourth Conference of the European Association of Internal Medicine (AEMIE) held in Strasbourg in April 1977.

References
Augur, N. A. Jr. (1970) Gastroenterology, 58, 311.
Baraona, E., Pirola, R. C. and Lieber, C. S. (1974) Gastroenterology, 66, 226.
Beaumont, W. (1833) Experiments and Observations on the Gastric Juice and the Physiology of Digestion. Plattsburg, New York: E. S. Allen.
Collins, C. H., Cook, P. J., Foreman, J. K. and Palfreman, J. F. (1972) Lancet, 1, 141.
Croft, D. M., Pollock, D. J. and Coghill, N. F. (1966) Gut, 7, 333.
Davenport, H. W. (1969) Gastroenterology, 56, 439.
Dinoso, V. P., Choy, W. Y., Sislet, H. and Lorber, S. H. (1970) American Journal of Digestive Diseases, 15, 809.
Halstead, C. H., Griggs, R. C. and Harris, J. W. (1967) Journal of Laboratory and Clinical Medicine, 69, 116.
Halstead, C. H., Robels, E. A. and Mezey, E. (1973a) American Journal of Clinical Nutrition, 26, 831.
Halstead, C. H., Robels, E. A. and Mezey, E. (1973b) Gastroenterology, 64, 526.
Israel, G., Kalant, H. and Lauder, I. (1965) Biochemical Pharmacology, 14, 1803.
Israel, G., Salazar, I. and Rosemann, E. (1968) Journal of Nutrition, 96, 499.
Israel, G., Valenzuela, J. E., Salazar, I. and Ugarte, G. (1969) Journal of Nutrition, 98, 222.
Johnston, S. J., Jones, P. F., Kyle, J. and Needham, C. D. (1973) British Medical Journal, 3, 655.
Joske, R. N., Finkh, E. S. and Wood, J. J. (1955) Quarterly Journal of Medicine, 24, 269.
Krasner, N. (1975) 'Some considerations of somatic presentations and treatment of alcoholism.' MD Thesis, University of Glasgow.
Krasner, N., Thomson, T. J., Crean, G. P. and McNeil, C. (1974) Gut, 15, 336.
Krasner, N., Cochran, K. M., Russell, R. J., Carmichael, H. G. and Thompson, G. G. (1976a) Gut, 17, 425.
Krasner, N., Carmichael, H. A., Russell, R. I., Thomson, G. G. and Cochrane, K. (1976b) Gut, 17, 249.
Lawrence, D. R. (1966) In Clinical Pharmacology, 3rd ed., p. 283. London: J. & A. Churchill.
Lindenbaum, J. and Lieber, C. S. (1969) Nature, 224, 806.
McGlashan, M. D. (1969) Gut, 10, 643.
Mezey, E., Jow, E., Slavin, R. E. and Tobon, F. (1970) Gastroenterology, 59, 657.
Mowat, M. A. G. and Brunt, P. (1976) In Recent Advances in Gastroenterology. (ed. I. G. D. Bouchier). Edinburgh and London: Churchill Livingstone.
Needham, C. D., Kyle, J., Jones, P. F., Johnston, J. J. and Kerridge, D. F. (1971) Gut, 12, 819.
O'Keane, M. J., Russell, L. I. and Goldberg, A. (1972) Journal of Alcohol, 7, 6.
Roberts, D. M. (1972) Gut, 13, 768.
Rubin, E., Ryback, B. J., Lindenbaum, J., Gerson, C., Walker, G. and Lieber, C. S. (1972) Gastroenterology, 63, 801.
Russell, R. I., Allan, J. G., Gerskovitch, V. P. and Robertson, J. W. K. (1972) Clinical Science, 42, 735.
Schoenberg, B. A., Bailor, J. C. and Foreman, J. K. (1971) Journal of the National Cancer Institute, 46, 43.
Small, M., Longarini, A. and Zamchek, N. (1959) American Journal of Medicine, 27, 575.
Smith, B. M., Shillman, J. J., Edwards, B. G. and Liley, W. (1971) New England Journal of Medicine, 285, 716.
Trefflot, M. J. (1975) American Journal of Gastroenterology, 63, 32.
Varis, K. (1971) Scandinavian Journal of Gastroenterology, 6, Suppl. 13, 1.
Vlahcevic, Z. R., Juttijudata, P., Bell, C. S. and Swell, L. (1972) Gastroenterology, 62, 1174.
Walker, J. E. C. and Gordon, E. R. (1970) Biochemical Journal, 119, 511.
Whitehead, L. (1973) In Mucosal Biopsy of the Gastrointestinal Tract. London: W. B. Saunders.
Book Review

Textbook of Medical Practice by J. Fry, P. S. Byrne and S. Johnson. MTP Press Ltd 1976. Price £9.95. 665 pages.

I approached this book with some trepidation as I felt my own lack of experience of family practice did not really equip me to judge a textbook devoted to it. But I believe that medicine is medicine, whether practised in hospital or in the community, and the same clinical approach and standards are needed for both. I must immediately say that I enjoyed reading this book and regard it as an important and useful contribution to medical teaching. In recognition of the high percentage of our graduates who enter general practice, most medical schools have now introduced some teaching in this field. This has usually consisted of exposing students to the type of clinical problems they are likely to encounter as general practitioners and perhaps emphasising that a hospital admission is often simply an episode in a longer illness. Most textbooks of medicine concern themselves solely or predominantly with 'hospital-diseases', which is not surprising since most are written by hospital consultants. Dr Fry and his colleagues have written about the common problems encountered in general practice. These are defined in Chapter 3 and care is taken not to lose sight of them throughout the book. It is pleasing to see the emphasis placed on clinical methods in the chapter by Professor Byrne. The book attempts to provide guidance about difficult decisions that are essentially those of the GP, such as which patients to refer to hospital and how to manage the rehabilitative aspects of illness. I have some minor quibbles: for instance, I would not agree with the enthusiastic advocacy of adrenal steroids for asthma (page 95), or the advice about using ACTH (page 96), and the treatment for pulmonary tuberculosis is not quite up-to-date. Occasionally, the writers get into real trouble, particularly in the more specialised chapters. In the gynaecology chapter, for instance, amenorrhoea is said to be caused by dwarfism and, more embarrassingly, by Klinefelter's syndrome. It is a pity to find these lapses, as this book should prove popular with both undergraduate and postgraduate students, and I think it is too good to be spoiled by this sort of carelessness. I am sure the editors will polish up future editions and I can see this emerging as an important and useful book.

R. Hoffenberg