the oncogenic effect of the virus. It may be, therefore, that interference with the immune mechanism is an important pre-requisite for successful carcinogenesis.

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[1] Foley, E. J., *Cancer Res.*, **13**, 578, 835 (1953). Prehn, R. T., and Main, J. M., *J. Nat. Cancer Inst.*, **18**, 769 (1957). Klein, G., Sjögren, H. O., Klein, E., and Hellström, K. E., *Cancer Res.*, **20**, 1561 (1960).
[2] Sjögren, H. O., Hellström, I., and Klein, G., *Cancer Res.*, **21**, 329 (1961). Klein, G., Sjögren, H. O., and Klein, E., *ibid.*, **22**, 955 (1962). Slettenmark, B., and Klein, E., *ibid.*, **22**, 947 (1962).
[3] Habel, K., *J. Exp. Med.*, **115**, 181 (1962).
[4] Sachs, L., *J. Nat. Cancer Inst.*, **29**, 759 (1962).
[5] Law, L. W., and Dawe, C. J., *Proc. Soc. Exp. Biol.*, **105**, 414 (1960).
[6] Linder, O. E. A., *Cancer Res.*, **22**, 380 (1962).
[7] Burnet, F. M., *Science*, **133**, 307 (1961). Prehn, R. T., in *Conceptual Advances in Immunology and Oncology, Sixteenth Symp. Fundamental Cancer Research*, Texas Univ. and M.D. Anderson Hosp. and Tumor Inst. (in the press).
[8] Miller, J. F. A. P., *Lancet*, ii, 748 (1961); *Ann. N.Y. Acad. Sci.*, **99**, 340 (1962).
[9] Vandeputte, M., Denys, J., Leyton, R., and De Somer, P., *Life Sciences* (in the press).

Wine as Source of Iron in Hæmochromatosis

The belief that there is increased absorption of iron from a normal diet in idiopathic hæmochromatosis is based on assumptions of normal dietary iron during the time the disease is developing. Studies of iron absorption late in the disease have led to conflicting conclusions[1,2]. This communication directs attention to wine as a possible source of increased dietary iron in hæmochromatosis.

A close association exists between the use of alcohol and hæmochromatosis; 20–80 per cent of hæmochromatotics are alcoholic. It may be inferred that additional patients consume alcohol in lesser quantities. Increased tissue iron has been found in 40–80 per cent of patients with 'alcoholic' or nutritional cirrhosis in several countries of the world[3–5]. The amount of iron may frequently be as great as in hæmochromatosis.

Investigations of the iron content of alcoholic beverages from various countries reveals that wine, in contrast to distilled beverages, is a rich source of iron, chiefly in the ferrous form, with an average of 4·4 mg/l. in U.S. varieties consumed most commonly by alcoholics in Boston; an average of 6·2 mg/l. was found in 22 French varieties from Burgundy, Bordeaux, and Romagne; and 10–16 mg/l. in cider and wine from Rennes, France, where iron diseases are especially common.

The iron appears to be derived chiefly from pipes and equipment used in preparation of wine, and is well known to the wine industries[6]. The copper content of French wines is approximately 1 mg/l., derived from copper sprays of the grapes and from equipment. Prior to the Second World War the iron content of U.S. wines was considerably higher, up to 35 mg/l. From about this time attention was directed in the wine industry to lowering the iron content because it is an important contributor to the formation of sediment, and the U.S. market prefers sediment-free wines. Chronic alcoholics in Boston consume large quantities of wine in preference to distilled spirits because it is cheap; 2 l./day is not unusual and is probably a minimum figure. Chronic alcoholics in France consumed an average of 2·5–5 l./day, and 50–116 non-alcoholic controls drank 1–2 l./day in an investigation[7].

The normal Western diet contains 10–15 mg/day of iron, of which approximately 10 per cent or 1–1·5 mg/day is absorbed and excreted. If iron is added to the diet it continues to be absorbed[8], resulting in increased body stores. Hæmochromatosis is a disease of middle age, and is characterized by a body store of 20 g or more of iron in contrast to the normal 4–5 g. Absorption of 1·8 mg. of iron a day over the normal amount for 30 years, or of 2·5 mg/day for 20 years accounts for the quantity of body iron in hæmochromatosis. With absorption of 17·8 per cent[8] of dietary iron, consumption of 2 l. of particular brands of present-day U.S. wines would result in absorption of 1·8 mg of iron. Non-alcoholic Frenchmen in Rennes consuming 2 l. of wine with 16 mg of iron/l. and with 15·1 per cent absorption[8] would absorb 5 mg. Alcoholic Frenchmen in Rennes consuming 5 l./day of the same wine, assuming 12·6 per cent absorption[8] would absorb 10 mg. It is possible that absorption would decrease with increased body stores, but even assuming 10 per cent absorption this would alter the foregoing figures to 0·8 mg iron for 2 l. of U.S. wine, 3 mg for 2 l. Rennes wine, and 8 mg for 5 l. of Rennes wine. Consumption of 2 l./day of U.S. wine prepared prior to the Second World War, with its iron content 30 mg/l., would result, with an absorption of 12·7 per cent[8] in absorption of 7·6 mg iron, and with 10 per cent absorption in 6 mg.

Ingestion of iron and copper containing wine or other beverages can explain the characteristic features of hæmochromatosis, and is consistent with the concept that it is a variant of nutritional or 'alcoholic' cirrhosis or of the factors that lead to cirrhosis[9]. The occasional familial occurrence of the disease, and of elevated serum or tissue levels of iron in relatives is commonly presumed to be due to genetic inheritance. Detailed dietary histories and personal dietary analysis have not been carried out during the developmental years of the disease, however, nor in family members. A familial occurrence of elevated serum or tissue iron in the presence of ingestion of a common dietary substance such as iron obviously need not be genetically determined. In as much as the source of iron in wine appears to be from equipment used in preparation, other alcoholic beverages, particularly from early years when iron equipment was more prevalent, or 'home made' alcoholic preparations, might be a rich source. Other factors in cirrhosis, such as diet, pancreatic disease, and anæmias, could further enhance iron absorption[9] but need not be invoked. Additional sources of oral iron are non-prescription medical preparations taken commonly in many countries, including the United States. The amounts of iron in wine and in medicines are not harmful, even when accumulated in large quantities in the liver, and so are not contra-indicated, but an understanding of the source of iron in hæmochromatosis will clarify many controversial beliefs about the disease, and about iron metabolism.

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[1] Alper, T., Savage, D. V., and Bothwell, T. H., *J. Lab. Clin. Med.*, **37**, 665 (1951).
[2] Chodos, K. B., Ross, J. F., Apt, L., Pollycove, M., and Halkett, J. A. E., *J. Clin. Invest.*, **36**, 314 (1957).
[3] Simmonds, M., *Berl. klin. Wchnschr.*, **46**, 591 (1909).
[4] Bell, E. T., *Diabetes*, **4**, 435 (1955).
[5] Pechet, G. S., and MacDonald, R. A., *New England J. Med.*, **6**, 267 (1962).
[6] Amerine, M. A., *Adv. Food Res.*, **8**, 133 (1958).
[7] *Nature*, **189**, 804 (1961).
[8] Smith, M. D., and Pannaccuilli, I. M., *Brit. J. Hæmat.*, **4**, 428 (1958).
[9] MacDonald, R. A., *Amer. Med. Assoc. Arch. Intern. Med.*, **107**, 606 (1961).