action by manufacturers and retailers. In the case of fire-
guards and oil heaters this was stimulated by Govern-
ment intervention. Up to the present the action on nightdresses has
been voluntary but now has legal backing. Underlying all
these developments is the standardization of fires for
which credit is particularly due to the British Standards
Institution and the Fire Research Station. Consumer organ-
izations have also helped in producing an informed public
demand for safer products.

Another example of successful control by manufacturers
was the substitution in 1957 of the explosive "thunder flash" type
of firework by a less dangerous "banger." This resulted in
reduction by two-thirds of the injuries due to these fireworks
being (wrongly) held in the hand (Jackson, 1961). However,
it is hard to see how the majority of firework accidents can be
prevented unless explosives are kept entirely out of the hands
of children and high-spirited teenagers.

In the light of the modest successes already achieved it
should be possible to tackle the remaining problems. These
include the more thorough guarding of open fires, provision of
safe nightwear for the elderly and infirm, and safer day-
wear, particularly for girls and women, though the relative
immunity of males has been reduced with the introduction of
unproofed cottons and cellulosics for trousers. New hazards
also may increase in importance—for instance, accidents with
flammable liquids are becoming more frequent, as also are
deaths from conflagration. These present new challenges to
research into details of causes and prevention.

Summary

Since the previous survey eight years ago both annual deaths
from burns and admissions to the Burns Unit have increased.
The main increases have been among persons aged 15 to
65 years.

Effect of Alcohol on Iron Absorption

T. H. BOTHWELL,* M.D., M.R.C.P.

Brit. med. f., 1964, 2, 1427–1429

There are several observations which suggest a relation between
excessive consumption of alcohol and the development of iron
overload. For example, approximately a third of the patients
exhibiting the full-blown clinical manifestations of idiopathic
haemochromatosis have a significant alcoholic background
(Sheldon, 1935; Finch and Finch, 1955). Furthermore, there is
evidence that alcoholsics as a group tend to have iron stores
such as have been found in the Bantu males of South Africa (Herbut
and Tamaki, 1946; MacDonald and Mallory, 1960). Finally, there is suggestive
evidence that the severity of the tissue siderosis so commonly
noted in the adult Bantu males of South Africa is closely
related to the drinking habits of these subjects (Seftel et al.,
1961).

There are several possible reasons for these various associa-
tions. In the first place, analyses of the home-brewed alcoholic
beverages consumed by the Bantu have revealed high iron
concentrations (Walker and Arvidsson, 1953), and it has been
calculated that many males ingest between 50 and 100 mg. of
iron daily from this source alone (Bothwell et al., 1964). A
similar, though less striking, association between iron and
alcoholic intakes has recently been pointed out by MacDonald
(1963), who has shown that most European and United States
wines contain significant amounts of iron. (For example, the
average iron concentration in French wines is 8.8 mg./l., and
in United States wines 4.9 mg./l.). A second possible way in
which excessive consumption of alcohol may lead to iron over-
load is through its pathological sequelae, such as chronic pan-
creatitis and chronic liver disease. Deficiency of the exocrine
secretions of the pancreas has been shown to be associated with
increased absorption of iron from the gut (Taylor et al., 1931;
Davis and Badenoch, 1962), and there is recent evidence indi-
cating that some subjects with cirrhosis of the liver absorb
iron excessively (Conrad et al., 1962; Callender and Malpas,
1963).
There are therefore several possible reasons why so many heavy drinkers have increased iron stores. However, one possibility has not been investigated—namely, that alcohol itself directly enhances iron absorption. The present investigation was carried out to try to answer this point.

**Material and Methods**

The absorption of 5 mg. of iron was assessed in 31 haematologically normal subjects and in four patients with histamine-fast achlorhydria. Because of the well-known variability in iron absorption from subject to subject, a double isotope technique was used in which each individual served as his own control. (The validity of this approach has been demonstrated in a previous communication (Jacobs et al., 1964).) The iron was administered in the fasting state. On one day it was dissolved in 250 ml. of water, and on the following day in 60 ml. of whisky or brandy, made up to a final volume of 250 ml. with water. In half the experiments the order of administration was reversed. Isotope labelling was with 70 μc of 56Fe on the one occasion and with 5 μc of 57Fe on the other. In different experiments the iron was administered as ferric chloride, as ferrous ascorbate (with 50 mg. of ascorbic acid), and as rat haemoglobin. Duplicate blood samples collected two weeks later were digested, electroplated on to copper disks, and differentially counted for the two isotopes as described previously (Bothwell and Finch, 1962). The relative percentage absorptions of the two doses were then calculated on the assumption that 80% of the iron absorbed from the gut was present in the red-cell mass at two weeks, and that the blood volume was 70 ml./kg. Results were therefore corrected by a factor of 10/8.

**Results**

The absorption of iron given as ferrous ascorbate was assessed in six normal subjects. The mean absorption was 18.8% in water and 17.5% in alcohol (see Table). There was also no

<table>
<thead>
<tr>
<th>Effect of Alcohol on the Absorption of 5 mg. of Iron Given as (A) Ferrous Ascorbate and (B) Haemoglobin</th>
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<tbody>
<tr>
<td>Without Alcohol</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td><strong>Percentage absorption</strong></td>
</tr>
<tr>
<td>21.7</td>
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<td>20.5</td>
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<td>22.5</td>
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<td><strong>Mean</strong></td>
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enhancement of the absorption of haemoglobin iron in the presence of alcohol, the mean figures in eight subjects being 14.9% in water and 13.4% in alcohol. In contrast, alcohol caused a marked increase in the absorption of iron given as ferric chloride. In 17 subjects the mean absorption in alcohol was 22.6%, as compared with 4.1% in water (see Chart). This effect could not, however, be demonstrated in four subjects with histamine-fast achlorhydria (a mean of 3.5% in water and 5.2% in alcohol).

**Discussion**

In a previous investigation the effect of hydrochloric acid on iron absorption was studied in subjects with histamine-fast achlorhydria (Jacobs et al., 1964). Hydrochloric acid was found to enhance markedly the absorption of ferric iron and to cause a modest increase in the absorption of ferrous iron. In contrast, haemoglobin iron absorption was not increased by acid. Although the reasons for these differences were not established, it seems likely that hydrochloric acid acts by maintaining ferric iron in solution until it reaches the absorbing area of the duodenum. The relatively small effect observed with ferrous iron is compatible with this thesis, since it is known that ferrous ions remain in solution at a much higher pH than do ferric ions (Hodgman et al., 1958). The fact that the absorption of haemoglobin iron is not increased by acid adds further weight to evidence obtained by other workers which suggests that this organic iron complex is absorbed in a manner different from simple iron salts (Turnbull et al., 1962).

In the present study alcohol was found to potentiate the absorption of ferric iron considerably, but to have no effect on the absorption of ferrous or haemoglobin iron. The similarity between these results and those obtained previously with hydrochloric acid suggested that alcohol might be exertiing its effect by stimulating the production of gastric acid. The fact that the administration of alcohol did not increase the absorption of iron in four subjects with histamine-fast achlorhydria would be compatible with this hypothesis.

Whether the present findings bear any relation to the pathogenesis of iron overload is still not clear. While it is known that excessive amounts of iron are present in the fermented beverages consumed by the Bantu (Walker and Arvidsson, 1953), it has not been possible to show an enhancement of absorption when iron has been administered in Bantu beer (Bothwell et al., 1964). However, it should be noted that the type of beer which was tested had a very low alcohol content (±3%), and it remains possible that the more potent adulterated drinks consumed by many of these subjects may enhance iron absorption significantly.

Recent evidence suggests that the present findings may have a wider relevance. It has been pointed out that many wines from different parts of the world contain significant amounts of iron, and it has been suggested that the high incidence of iron overload in alcoholic subjects is a result of the excessive iron intake (MacDonald, 1963). It should, however, be noted that wines contain 10–20% alcohol, and the absorption of iron taken in this way may thus be enhanced.

These considerations do not exclude the possibility that other factors may contribute to the association between iron overload and the excessive consumption of alcohol. Pancreatitis is common in alcoholics, and there is now good evidence that deficiency of the exocrine secretions of the pancreas is associated with excessive absorption of iron. This has been shown in animals after pancreatectomy (Taylor et al., 1931), ligation of the pancreatic duct (Taylor et al., 1935; Gillman et al., 1947; Kinney et al., 1950), and ethionine-induced pancreatic damage (Kinney et al., 1953), and in patients with chronic pancreatitis.
(Davis and Badenoch, 1962). Furthermore, there is evidence that the increased absorption can be reduced by the giving of pancreatic extract (Kinney et al., 1950; Davis and Badenoch, 1962; Saunders et al., 1963). The fact that cirrhosis is common in alcoholics may also be of relevance, since it has been shown that some cirrhotic subjects absorb excessive amounts of iron even when the body stores are normal or increased (Conrad et al., 1962). It is, however, still not clear whether these effects are secondary to the cirrhosis itself or to associated pancreatic damage (Callender and Malpas, 1963).

Lastly, alcoholics as a group eat suboptimal diets, and there are several experimental studies showing increased absorption of iron when the diet is low in certain nutrients but high in iron. These diets have included low phosphate (Hegsted et al., 1949), low protein, high fat (Kaufman et al., 1958), and choline-deficient (MacDonald, 1960) regimes.

With all these factors contributing to the excessive absorption of iron it is not surprising that doubt has been cast on whether idiopathic haemochromatosis occurs as a distinct entity. The arguments against its existence have been presented by MacDonald (1961, 1963), who believes the condition to be a variant of alcoholic cirrhosis occurring in subjects exposed to high iron diet. Some support for this suggestion is provided by the fact that many patients presenting with the disease have a background of alcoholism (Sheldon, 1935; Finch and Finch, 1955). There is, however, a strong body of evidence, accumulated from many sources, which indicates the existence of a specific metabolic disorder in which excessive amounts of iron are absorbed from a normal diet.

Firstly, it should be emphasized that a large number of reported patients with the disease have not been alcoholic, and no other source of excessive dietary iron has been uncovered in these cases. Secondly, there are several family studies in which varying degrees of iron overload have been demonstrated in relatives of patients with haemochromatosis, thus supporting the concept of an inherited metabolic disorder (Bothwell et al., 1959; Williams et al., 1962). The fact that only a proportion of siblings living in the same household have shown increased stores can also be taken as evidence against the idea that some environmental factor, such as a high dietary intake, is essential in pathogenesis. Thirdly, it has been possible to show an abnormally high absorption of radioactive iron in some patients with the fully developed disease (Alper et al., 1951; Bothwell et al., 1953). This is especially so in young subjects, and the failure to demonstrate increased absorption in some older patients may well be due to the inhibitory effect exerted by the enormous iron stores. Support for this contention has been provided by the finding of very high absorption rates in such individuals after reduction of stores by repeated phlebotomy. This has been noted at a time when the haemoglobin level was normal and the serum iron normal or even raised (Pirri-Biroli et al., 1958).

Although consideration of these various findings suggests the existence of a specific metabolic disorder resulting in excessive iron absorption, it is probable that only a proportion of affected individuals develop the clinical manifestations of haemochromatosis. The size of the accumulated iron deposits in any particular case must depend upon a number of factors. These include the degree to which the absorptive rate deviates from the normal, the amount of iron in the diet, the duration of the period of increased absorption, and the quantity of iron lost from the body. On this basis the excessive intake of iron, particularly when present in alcohol, might be expected to accelerate the development of the full clinical syndrome in subjects who would otherwise have remained asymptomatic.

**Summary**

Alcohol in the form of whisky or brandy markedly increased the absorption of ferric chloride in normal subjects, but had no effect upon the absorption of ferrous ascorbate or haemoglobin iron. Some evidence was obtained to suggest that this action was due to the stimulation of hydrochloric acid production in the stomach.

These findings may have some relevance to the well-established association between excessive consumption of alcohol and the development of iron overload.

This study was supported in part by a grant (AM 04912-03) from the National Institutes of Health, U.S.A., and in part by grants from the Council for Scientific and Industrial Research and the Atomic Energy Board, South Africa.

**REFERENCES**


--- Arch. intern. Med., 107, 606.


