LIVER IRON STORES IN DIFFERENT POPULATION GROUPS IN SOUTH AFRICA

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SUMMARY
The hepatic non-haem iron concentrations of 1143 subjects dying in Durban, Pretoria and Cape Town were determined. The effects of certain disease processes upon liver iron stores were confirmed, and data from subjects dying from such diseases were excluded. No significant differences were revealed between comparable groups from the 3 cities. In Whites and Bantu, the median values were higher in adult males than in postmenopausal females, and lowest in premenopausal females, reflecting the greater iron requirements imposed by menstruation and pregnancy. The figures in the Bantu were significantly higher than those in the corresponding members of each of the other population groups. In addition, suggestive evidence was obtained that a significant proportion of Coloured males have iron stores that are lower than normal.

In contrast to the situation in adults, significantly lower concentrations were found in Bantu children than in White children. The probable explanation for these observations is that the Bantu children are not exposed to the major source of superfluous dietary iron, namely the home-brewed beers.

In states of frank iron deficiency, all the available body iron is incorporated into functional compounds such as haemoglobin and iron-containing enzymes. 1, 2 When, however, there is enough iron to satisfy all functional requirements, any surplus is stored as ferritin and haemosiderin.

APPENDIX IV. CALCULATIONS FOR CONSUMPTION OF SUGAR IN
HOUSEHOLDS PER MAN-UNIT PER DIEM

<table>
<thead>
<tr>
<th>Product</th>
<th>Firm</th>
<th>Percentage of added sugar</th>
<th>Sugar content in g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condensed milk</td>
<td>Nestlé</td>
<td>44%</td>
<td>172 g per 14-oz tin</td>
</tr>
<tr>
<td>Ice-cream</td>
<td>Wall</td>
<td>10% - 12%</td>
<td>40 g per pint</td>
</tr>
<tr>
<td>Soft drinks</td>
<td>Coca Cola</td>
<td>85 g per 'Family size' (770 ml)</td>
<td>33 g per 'King size' (300 ml)</td>
</tr>
<tr>
<td>Fruit squash</td>
<td>Safari</td>
<td>30%</td>
<td>218 g per 26-oz bottle</td>
</tr>
<tr>
<td>Fruit squash</td>
<td>Tropical Fruits</td>
<td>1 lb : 2 pt juice</td>
<td>218 g per 26-oz bottle</td>
</tr>
<tr>
<td>Canned fruit</td>
<td>Langeberg</td>
<td>15% approx. (depending on fruit)</td>
<td>68 g per 1-lb tin</td>
</tr>
<tr>
<td>Jelly</td>
<td>Royal</td>
<td>80%</td>
<td>80 g per packet (100 g)</td>
</tr>
<tr>
<td>Instant pudding</td>
<td></td>
<td>70%</td>
<td>70 g per packet (100 g)</td>
</tr>
<tr>
<td>Regular pudding</td>
<td></td>
<td>60% - 70%</td>
<td></td>
</tr>
<tr>
<td>Pie filling</td>
<td></td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>

in the liver, spleen and bone marrow. It is thus apparent
that the amount of storage iron present at any one time
reflects the nutritional status of an individual in so far as
iron is concerned. Because of this, several methods have
been developed for assessing the body-iron stores. These
include the histological estimation of the amount of visible
iron and the chemical determination of tissue-iron con­
centrations.1 Some caution must, however, be exercised in
this regard, since various non-nutritional factors may
modify either the amount or the distribution of iron
within the body. For example, in malignant neoplasms
the iron from catabolized haemoglobin is not released from
reticulo-endothelial cells at a normal rate; as a result
anaemia develops, and an increased proportion of total
body iron is present in the stores.2 Estimation of the
storage-iron content of the body in such subjects gives
a falsely optimistic picture of their iron nutrition. In
this previous study evidence was obtained that distortion
of this type is more than merely a theoretical possibility.2 A
digital computer was used to analyse the non-haem iron
concentrations in 3 983 specimens of liver obtained from
26 different countries, and the influence of certain non-
nutritional factors such as the cause of death was estab­
lished. At the same time it was apparent that valid
information could be obtained with this approach, pro­
vided that allowances were made for these distorting
factors.

Deficiency of iron is a major nutritional problem in
many countries, while excessive stores of iron are en­
countered only rarely. Iron overload of varying degrees is,
however, extremely common in the adult Bantu popula­
tion of Southern Africa. The condition, which appears to
be due to the presence of large amounts of tonic iron in
home-brewed alcoholic beverages, has been extensively
investigated by a number of workers over the years.4-8 The
iron nutrition of other ethnic groups has also been
assessed, but only two studies have been reported in
which specimens from different parts of the Republic were
compared.9,10 Moreover, most of the available information
on iron nutrition has been obtained by histological
methods, and while this approach can undoubtedly be
semi-quantitative, it lacks the precision of chemical ana­
lysis. For these reasons it was thought worth while to
obtain necropsy specimens of liver from different parts of
the Republic for estimation of the non-haem iron con­
centrations.

Materials and Methods

Specimens of liver weighing 3 - 5 g were obtained at
necropsy from a total of 1 143 subjects, preserved in
buffered formal saline, and transported to Johannesburg
for analysis. The storage-iron concentrations were esti­
lated on 1-g aliquots by the method of Torrance and
Bothwell.11 The age, sex and cause of death were recorded
in each case. The findings in a limited number of children
aged between 4 months and 18 years were analysed
separately. Women were considered to be premenopausal
if they were aged 39 years or less, and postmenopausal if
aged 50 years or more; data from female subjects aged
40 - 49 years were discarded. The data were classified into
4 categories on the basis of the cause of death, 2 of which
would be expected to influence the hepatic storage-iron
content and 2 of which would not. The categories were
respectively malignant neoplasms, uraemia and chronic
infections, acute trauma, and finally diseases such as cere­
bral thrombosis, acute pneumonia, etc. All the information
was entered onto cards and analysed by means of a digital
computer.

Results

The numbers of specimens from subjects in the different
groups, together with the median hepatic non-haem iron
concentration for each group, are set out in Table I.

Adults

Effect of cause of death. Storage-iron concentrations
have been shown to increase with age in Bantu males, but
in White males this does not occur.9 In women of all races
the menopause produces an age-linked effect. Only
adult White males could therefore be used to examine the
possible effects of the various causes of death upon hepatic
storage-iron concentrations, and only the Pretoria group
was large enough. Analysis of variance showed that the
values in those subjects who died from malignant neo­
plasms and from chronic infections or uraemia were sig­
ificantly greater than in those who died from the re­
maining natural causes or from trauma (Table II). Since
there was reason to believe that the values in the first
group were higher as a result of the redistribution of body
iron rather than an increase in the total amount, they
were excluded from the remainder of the analysis of the
adult data.

Effect of geographical location. No evidence was ob­
tained that significant differences existed between the
values from the 3 different cities, in either White or Bantu
subjects (Table III).

Comparison between different races. The data from the
3 cities were pooled to permit a comparison between the
different racial groups. In males and in post- and pre­
menopausal females, the storage iron concentrations in the
livers from Bantu subjects were significantly higher than
those from Whites, Coloureds or Indians (p<0.001) (Table
IV). No significant differences between the last 3 groups
were demonstrated, with the exception of the Coloured
males. The low median concentration in this group (109
µg/g) suggested that there might be a significant number of
individuals with very low iron stores. Accordingly, a
direct comparison between White and Coloured males was
undertaken. Of the 133 White males, only 29 had hepatic
non-haem iron concentrations lower than 100 µg/g, com­
pared with 15 of the 34 Coloured males. This difference
was significant (Chi squared, 5.85: 0.02>p>0.01).

Comparison between premenopausal and postmenopau­
sal females. Median values were lower in premenopausal
Bantu, White and Coloured women, but the difference was
significant only among the Bantu (p<0.001) (Table V).
(There were insufficient data in the case of Indians.)

Children

The number of specimens available for analysis was
unfortunately small, and in most cases comparisons were
only possible if no data were excluded on the basis of
cause of death.

Comparison between males and females. Enough data
were available from Bantu children in Durban and in
**Comparison between children aged 4 months - 10 years and those aged 11 - 18 years.** In neither girls nor boys among the Bantu children could a significant difference be demonstrated between those aged 10 years or younger and those aged 11 years or older. Among the girls, the numbers with hepatic non-haem iron concentrations less than 200 µg/g were 13 out of 21 in the younger Durban group and 5 out of 9 in the older (Chi squared, 0·1: p>0·1), while in the corresponding groups from Pretoria the figures were 17 out of 25 and 6 out of 10 (Chi squared, 0·2: p>0·1). In the younger Durban boys, 14 of 26 were below 200 µg/g compared with 5 of 13 older boys (Chi squared, 0·8: p>0·1), while the figures in the Pretoria boys were 13 out of 26 and 4 out of 8 (Chi squared 0·0).

**Comparison between Bantu children from Pretoria and those from Durban.** Since no effect of either age or sex had been established, the observations were pooled, and a comparison was made between the Bantu children from Durban and those from Pretoria. However, no significant difference was demonstrated. Of the 69 Durban children, the hepatic non-haem iron concentration was lower than 200 µg/g in 37, compared with 40 out of 69 in the Pretoria children (Chi squared, 0·26: p>0·1).

**Comparison between Bantu and White children.** There were unfortunately not enough observations on Indian or Coloured children to permit a comparison between all 4 ethnic groups, but there were 44 specimens from White Pretoria children which could be compared with 69 Bantu children from Pretoria (Table VI). There was a highly significant difference (p<0·001), the Bantu values being lower than those in Whites. Inspection of the data showed, however, that a somewhat higher proportion of the White specimens had come from subjects dead from malignant neoplasms, uraemia or chronic infections than was the case with the Bantu children. Since the difference in storage-iron concentrations between the two groups might possibly have been due to this rather than to nutritional factors, a second comparison was made after excluding such observations from both groups. When this was done, a significant difference was still present, but it was considerably smaller (p<0·05). The median values in the White and Bantu groups were 357 µg/g and 117 µg/g respectively when all the observations were included, and only 150 µg/g and 100 µg/g after the neoplasms, etc. had been omitted.

**Discussion**

Ever since Strachan" reported that iron overload was common in the adult Bantu population of South Africa, the condition has been studied by a number of investigators in different parts of the Republic. In several of the earlier reports the quantity of iron present in the liver was assessed histologically. However, the criteria used to judge the degree of siderosis varied from observer to

### Table I

<table>
<thead>
<tr>
<th>Subjects dying from malignant neoplasms, uraemia or chronic infections</th>
<th>Bantu</th>
<th>White</th>
<th>Coloured</th>
<th>Indian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median iron (µg/g)</td>
<td>89</td>
<td>163</td>
<td>136</td>
<td>119</td>
</tr>
<tr>
<td>Neoplasms, etc. excluded</td>
<td>11</td>
<td>16</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>All causes of death</td>
<td>11</td>
<td>16</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Median iron (µg/g)</td>
<td>8</td>
<td>13</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Neoplasms, etc. excluded</td>
<td>8</td>
<td>13</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>All causes of death</td>
<td>8</td>
<td>13</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Median iron (µg/g)</td>
<td>101</td>
<td>136</td>
<td>119</td>
<td>86</td>
</tr>
<tr>
<td>Neoplasms, etc. excluded</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>All causes of death</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Median iron (µg/g)</td>
<td>66</td>
<td>188</td>
<td>119</td>
<td>86</td>
</tr>
</tbody>
</table>
observer, so that only approximate comparisons can be made between the results obtained in different studies. In addition, the material was often selected in one way or another, so that it is not possible to obtain an accurate picture of the incidence of siderosis in the population as a whole. Moreover, while it has been shown that the size of the stores can be satisfactorily judged by histological methods in subjects with iron overload, the technique is not sensitive enough to provide an assessment of iron nutrition in non-siderotic individuals. The alternative, and more satisfactory approach of quantitative chemical analysis has been applied in several studies. 

Bothwell and Bradlow determined the iron concentrations in the livers of 147 Bantu subjects (16 females) dying of acute trauma in Johannesburg. Only 35% of these individuals had hepatic iron concentrations within or slightly above the range regarded as normal in other populations, i.e. less than 0.2% dry weight (approximately 400 \( \mu g/g \) wet weight). Bothwell and Isaacson carried out a similar study on 318 Bantu males and 265 Bantu females dying in hospital in Johannesburg from unspecified causes. Values less than 0.2% dry weight were found in 29.6% of the males. In the present investigation concentrations below 400 \( \mu g/g \) wet weight were found in 30.7% of the Bantu males.

The similarity of these figures might suggest that undue preoccupation with the theoretical effects of non-nutritional factors upon hepatic iron concentrations is unwarranted; however, this is probably only true when the majority of the population has abnormally large stores of iron, as in the Bantu. Under such circumstances the effects of pathological processes upon the size or distribution of the body-iron stores are masked. That the influence of such factors cannot be ignored in non-siderotic populations was illustrated in the present investigation. In the 44 White children from Pretoria, the median hepatic storage-iron concentration was 357 \( \mu g/g \), but when the 20 observations obtained from individuals who had died from neoplasms, chronic infections or uraemia were excluded, the median figure was only 150 \( \mu g/g \) (Table VI). In Bantu children the effects of excluding this group were similar but less marked. Estimating the hepatic storage-iron concentration in subjects with such diseases gives a falsely high picture of the iron nutritional status because the iron from catabolized haemoglobin is not released into the plasma at a normal rate, and accumulates in reticuloendothelial cells in the liver and elsewhere.

The sex of the subjects is another factor which must obviously be taken into consideration when iron nutrition is assessed. In women the increased iron requirements associated with menstruation and pregnancy mean that more iron has to be obtained from the diet if the individual is to stay in balance. Since the amount of available iron in the diet is nearly always limited, it is to be expected that iron stores in premenopausal women will be smaller than those in men, and also smaller than those in postmenopausal women. This was confirmed in the present study, and it is therefore obvious that valid comparisons between groups of women cannot be made unless this factor is taken into account.

The effect of age must also be considered. Older women have greater concentrations of storage iron than younger women, but this is due rather to the menopause than to a direct effect of age itself. Age has previously been shown not to influence storage-iron concentrations in males from a number of different countries. The excretion of iron from the body in healthy males varies within relatively narrow limits, and the regulation of iron balance is achieved by adjusting absorption to meet requirements. Since it is known that the average western type of diet contains more available iron than is needed by adult males, the finding that body-iron stores in old men are no larger than in young men testifies to the efficiency of the intestinal mucosal mechanisms for excluding super-

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Trauma</th>
<th>Cardiovascular, etc.</th>
<th>Neoplasms</th>
<th>Chronic infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretoria White males</td>
<td>182</td>
<td></td>
<td>-2.58</td>
<td>+1.56</td>
<td>+1.61</td>
</tr>
<tr>
<td>Pretoria Bantu males</td>
<td>110</td>
<td></td>
<td>-0.02</td>
<td>+0.58</td>
<td>-1.16</td>
</tr>
<tr>
<td>Durban Bantu males</td>
<td>171</td>
<td></td>
<td>+0.71</td>
<td>-0.04</td>
<td>+1.30</td>
</tr>
</tbody>
</table>

TABLE III. EFFECT OF GEOGRAPHICAL LOCATION ON HEPATIC NON-HAEM IRON CONCENTRATIONS (NEOPLASMS, URAEMIA AND CHRONIC INFECTIONS EXCLUDED)

<table>
<thead>
<tr>
<th>Group</th>
<th>City</th>
<th>No. in group</th>
<th>No. with hepatic iron &lt;200 ( \mu g/g )</th>
<th>Chi squared</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>White males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretoria</td>
<td>Cape Town</td>
<td>37</td>
<td>17</td>
<td>0.72</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td></td>
<td>Pretoria</td>
<td>96</td>
<td>52</td>
<td>0.46</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Bantu males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretoria</td>
<td>Cape Town</td>
<td>8</td>
<td>4</td>
<td>2.26</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td></td>
<td>Durban</td>
<td>133</td>
<td>19</td>
<td>0.35</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Bantu postmenopausal females</td>
<td>Pretoria</td>
<td>10</td>
<td>3</td>
<td>0.10</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td></td>
<td>Durban</td>
<td>15</td>
<td>3</td>
<td>0.10</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Bantu premenopausal females</td>
<td>Pretoria</td>
<td>39</td>
<td>23</td>
<td>0.10</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td></td>
<td>Durban</td>
<td>36</td>
<td>20</td>
<td>0.10</td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>

TABLE II. EFFECT OF CAUSE OF DEATH ON HEPATIC NON-HAEM IRON CONCENTRATIONS

Analysis of variance
fluous iron. The mucosa is not, however, able to reject all unwanted iron if very large amounts are ingested. This has been demonstrated in experimental animals and in the clinical situation it is manifested both by acute iron poisoning and by the development of siderosis in subjects such as the Bantu who are continually exposed to excessive amounts of ionic iron in the diet.

There does not appear to be any a priori reason why iron nutrition should vary in the different centres of the Republic. Examination of the results obtained in the histological study carried out in Cape Town by Uys and co-workers and that performed by Wainwright in Durban suggests that there are no striking differences between the Bantu in the two cities, once allowance has been made for the varying histological criteria. The only previous studies in which any direct comparison was made between specimens from different parts of the Republic were those of Mayet and Bothwell and Charlton and co-workers. Mayet and Bothwell measured non-haem iron concentrations in liver specimens from Durban and Johannesburg; the majority of the subjects in their study had been killed by acute trauma. In that investigation the median value in the 81 Bantu males from Johannesburg was 966 μg/g, and in the 239 from Durban 786 μg/g, compared with 845 μg/g in the 218 Bantu males from all 3 centres analysed in the present investigation. Charlton and co-workers obtained a median hepatic iron concentration of 946 μg/g in 79 Bantu males from Johannesburg, and 776 μg/g in 234 from Durban. When the wide range of hepatic non-haem iron concentrations found in the Bantu is taken into account, these figures are remarkably close.

Very few observations on subjects belonging to other racial groups have been reported. Mayet and Bothwell found a median figure of 268 μg/g in White males from the two cities combined, compared with 198 μg/g in the present study, while in the investigation by Charlton and co-workers the value was 258 μg/g in 73 subjects from Johannesburg. The median figures for Indian males (Durban) were very similar in all three studies, namely 173 μg/g, 188 μg/g and 183 μg/g respectively. These figures may be compared with those found in males from other parts of the world. The median concentrations were 126 μg/g in Swedes, 186 μg/g in subjects from Seattle, USA, and 113 μg/g and 143 μg/g in individuals from two different hospitals in London. In Indians from New Delhi the median concentration was only 93 μg/g. From these observations it appears that the iron nutrition of White and Indian male South Africans is at least as good as that in a number of other countries. Unfortunately not enough observations were made on Coloured subjects in the present study for any firm conclusions to be reached. However, it may be noteworthy that a significantly larger proportion of Coloured males had hepatic iron concentrations less than 100 μg/g than did White subjects. In a previous histological survey Uys and co-workers showed that a portion of Coloured males had increased iron stores. The present results suggest that this population group may also include significant numbers with decreased iron stores. No final conclusions can, however, be reached until a more definitive study has been done on a larger number of subjects.

<table>
<thead>
<tr>
<th>Race</th>
<th>Ethnic Group</th>
<th>No. in Group</th>
<th>Median non-haem iron (μg/g)</th>
<th>No. with liver iron &lt;400 μg/g</th>
<th>All groups (p &lt; 0.001)</th>
<th>Chi squared (corrected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bantu, White and Coloured males, White males</td>
<td>786</td>
<td>16</td>
<td>0.16 (p &lt; 0.10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bantu males</td>
<td>218</td>
<td>15</td>
<td>27</td>
<td>48</td>
<td>15</td>
<td>6</td>
</tr>
</tbody>
</table>
A limited amount of information is available from previous studies with regard to the amounts of storage iron in the livers of women in the Republic. As with the males, most of the studies have been concerned with the incidence and severity of siderosis in the Bantu, and it is generally agreed that while marked iron overload undoubtedly occurs in women, it is less common than in men. For example, Bothwell and Isaacson found that hepatic iron concentrations were within or just above the normal range (up to 0.19%) in 75.4% of 265 Bantu females dying in hospital, while the comparable figure in males was 29.6%. A tendency for the concentration to rise with age was noted. In Wainwright's study only 2-3% of Bantu women below 40 years had severe hepatic siderosis compared with 24-31% of males, but in females over 50 years the figure was 48%. Severe siderosis is less common in Bantu women than in men because the major source of the excessive dietary iron is the home-brewed beers, which are less often consumed in quantity by the females. The median hepatic non-haem iron concentration in both pre- and postmenopausal Bantu women was nevertheless found to be significantly higher than the equivalent figures in other races (Table IV). There are almost no data from previous studies with which these values can be compared. Charlton and co-workers found a median hepatic iron concentration of 496 μg/g in 19 postmenopausal Bantu women, a figure similar to that found in the present study (409 μg/g). The women in Mayet and Bothwell’s study were not divided into pre- and postmenopausal groups.

The median value for postmenopausal White females in the present study (163 μg/g) may be compared with the figures for Sweden (120 μg/g), Czechoslovakia (170 μg/g), Seattle, USA (133 μg/g), and St George's Hospital, London (119 μg/g). No data for premenopausal women are available for comparison.

Very few observations on children have been reported; however, Wainwright found a mean hepatic non-haem iron concentration of approximately 0.06% dry weight in 13 Bantu children aged 6 months to 7 years, a figure not dissimilar from that found in the present investigation (100 μg/g wet weight). In view of the high storage-iron concentrations in Bantu adults, the fact that the median value in Bantu children was significantly lower than that in White children (150 μg/g) is striking. It seems reasonable to conclude that the diet consumed by Bantu children contains less available iron than is present in the White children’s diet.

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BOEKENTWANG : BOOKS RECEIVED