Alpha-1-antitrypsin genetic polymorphism in South Africa


Summary

The α₁-antitrypsin (AAT) or protease inhibitor (Pi) genetic polymorphism was studied in 144 white, 100 coloured, 104 Indian and 127 black (Northern Sotho) healthy individuals (controls), in the Pretoria area. Their Pi phenotype and gene frequency distributions are compared with world-wide data on other population groups. The severely deficient Pi phenotypes S, Z and SZ jointly attain frequencies of 0.3 - 0.4% in coloureds and whites; in blacks and Indians the corresponding frequencies are much lower. The implication for preventive medicine and public health is that in South Africa the sequelae of Pi deficiencies such as cirrhosis of the liver and/or emphysema of the lung are of practical importance in whites and coloureds and much less so in blacks and Indians. In 176 white breast cancer patients studied, the Pi phenotype and gene frequency distributions were found to be similar to those of healthy controls (not statistically significant). Cohorts of other patients were also phenotyped because of their low α₁-globulin concentrations in routine serum protein electrophoresis and/or their specific disease condition (cirrhosis of the liver or emphysema of the lung) known to be associated with AAT deficiency. These results are discussed in terms of their significance for family follow-up, genetic counselling and a preventive service. The need to avoid atmospheric pollution, especially cigarette smoke, is emphasised as a major and cost-effective preventive measure.


The plasma antiprotease α₁-antitrypsin (AAT) is well known for its broad-spectrum inhibitory function against a variety of proteolytic enzymes such as trypsin and, particularly, the neutrophil protease elastase. After the first description of a genetically determined AAT deficiency in 1963, it soon became evident that this plasma protein exists in many multimolecular forms. The pattern of manifestation of AAT is explained by a single Pi locus, assigned to chromosome 14, and by co-dominant gene expression. The M protein (subdivided into at least three forms: M1, M2 and M3) associated with normal Pi is commonest; the other isoproteins are less frequent and mostly abnormal variants. Among these the Z and S proteins continue to attract scientific interest because of the relatively high frequencies of the corresponding Pi*Z and Pi*S allelic genes in European populations and their causative association with specific diseases.1-3

The abnormal Pi*Z allelic gene is characterised by a point mutation, giving rise to a Z protein with the single amino acid substitution glutamic acid to lysine at position 342. In individuals with the PiZZ genotype, some Z protein accumulates in the liver, thus predisposing them to disease of this organ. These individuals also suffer from a deficiency of circulating AAT. The resultant insufficient protection, especially of lung elastin against digestion by proteases, can lead to the manifestation of destructive lung disease.4,5,7,8-12 The point mutation in the S protein leads to the amino acid substitution glutamic acid to valine at position 264. Accelerated catabolism of the altered molecules is seen as the cause for the reduced AAT plasma concentrations observed in individuals with the homozygous PiSS genotype. Consequently liver lesions are not a characteristic feature in these individuals, but the AAT deficiency can lead to destructive lung disease.4,5,7,8-12 The genotypes of most practical importance therefore are the homozygotes PiZZ and PiSS, attaining 10-15% and 50-60% respectively of normal plasma concentrations recorded as about 1,3 - 2,0 g/l. The respective heterozygotes, PiMZ and PiMS, have corresponding intermediate plasma concentrations.5,7,8

Ever since the first report of AAT deficiencies, their association with disease has remained a topic of continued medical as well as ecogenetic interest. The specific ecogenetic importance is derived from the observation that the manifestation of pathological conditions is greatly accelerated by environmental factors. This finding offers opportunities for prevention which are both cost-effective and practically feasible. For this reason the genetic forms of AAT deficiencies feature prominently among the topics of preventive medico-ecogenetic services, as advocated in some Western countries.4,5,7,10-12 In South Africa the genetic forms of AAT deficiencies have as yet not been systematically studied. This study was designed to help to fill this gap and thereby to support the development of an effective service for secondary prevention by early genetic diagnoses and appropriate counselling.

Populations, patients and methods

The population samples studied for Pi phenotypes were: (i) 127 blacks belonging to the Pedi ethnic group; (ii) 104 Indians from Pretoria; (iii) 100 coloureds from Pretoria (all these individuals were healthy women attending antenatal clinics where blood specimens are collected for various routine tests; aliquots were obtained for Pi phenotyping); and (iv) 144 whites from Pretoria.

Patients were assembled by two procedures:1

1. From all specimens sent to a general pathology laboratory (from hospital patients suffering from a variety of diseases), cases

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were selected when routine serum protein electrophoresis showed weak α1-bands. The AAT concentrations of these specimens were then measured by immunodiffusion assays. Those specimens with an AAT level under 40% of the normal plasma concentration (an arbitrary cut-off value) were then selected for Pi phenotyping. As expected, a large proportion of them had genetic Pi deficiency variants. These particular patients were then identified retrospectively with regard to their specific diseases. Among the cohort thus phenotyped, several were found to have lung or liver disease and others to have breast cancer (see below).

2. Specimens were received from patients known to suffer from a condition associated with AAT deficiency, i.e. lung or liver disease, and on whom Pi phenotyping was requested as a diagnostic test.

Thus three groups of patients were studied with regard to their Pi phenotypes: (i) 12 patients with lung disease or impaired lung function; (ii) 6 patients (mainly young children) with liver disease; and (iii) 12 patients with other conditions, mainly breast cancer. Since several of the first group of patients with Pi deficiency variants were identified as suffering from breast cancer, it was decided to phenotype a sufficiently large sample (176 patients) with this condition (and unselected for low AAT levels). In addition to the patient samples, a small group of asymptomatic relatives were also phenotyped. They represent family members of 'affected' patients, i.e. of patients with a Pi deficiency, mostly PiZ homozygotes, who serve as index cases for high-risk families, for the purpose of follow-up studies. The Pi phenotyping was performed by iso-electric focusing on commercially available polyacrylamide gels (pH gradient 4-5).

Results

Pi phenotypes in healthy controls

Table I shows that the frequency of the normal Pi*M phenotype (i.e. the two homozygotes M1 and M2 and the heterozygote M1M2) ranges from 84% to 87% in all South African population groups. The expected values were calculated using the Hardy-Weinberg equilibrium. The observed and expected frequencies are shown in Table I. The differences between the total numbers observed and expected are due to the fact that certain rare, expected phenotypes are not included in the expected totals, i.e. Pi*SVar, Pi*ZVar and PiVar (homozygote).

<table>
<thead>
<tr>
<th>Population samples</th>
<th>No. M1</th>
<th>M1M2</th>
<th>M2</th>
<th>M1S</th>
<th>M1Z</th>
<th>M2S</th>
<th>M2Z</th>
<th>M1Var*</th>
<th>M2Var*</th>
<th>S</th>
<th>Z</th>
<th>SZ</th>
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</thead>
<tbody>
<tr>
<td>South African whites</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Observed</td>
<td>144</td>
<td>92</td>
<td>30</td>
<td>2</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Expected†</td>
<td>143.75</td>
<td>92.64</td>
<td>29.68</td>
<td>2.38</td>
<td>9.63</td>
<td>3.21</td>
<td>1.54</td>
<td>0.51</td>
<td>3.21</td>
<td>0.51</td>
<td>0.250</td>
<td>0.0278</td>
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<td>Expected (%)</td>
<td>86.60</td>
<td>6.69</td>
<td>2.23</td>
<td>1.07</td>
<td>0.35</td>
<td>2.23</td>
<td>0.35</td>
<td>0.1736</td>
<td>0.0193</td>
<td>0.1159</td>
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<tr>
<td>(breast cancer)</td>
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<tr>
<td>Observed</td>
<td>176</td>
<td>116</td>
<td>32</td>
<td>4</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Expected†</td>
<td>175.81</td>
<td>117.00</td>
<td>33.43</td>
<td>2.39</td>
<td>8.15</td>
<td>8.98</td>
<td>1.16</td>
<td>1.28</td>
<td>2.44</td>
<td>0.35</td>
<td>0.1420</td>
<td>0.1719</td>
</tr>
<tr>
<td>Expected (%)</td>
<td>86.83</td>
<td>4.63</td>
<td>5.10</td>
<td>0.66</td>
<td>0.73</td>
<td>1.39</td>
<td>0.20</td>
<td>0.0807</td>
<td>0.0977</td>
<td>0.1778</td>
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<tr>
<td>combined†</td>
<td>320</td>
<td>208</td>
<td>62</td>
<td>6</td>
<td>20</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Expected†</td>
<td>319.55</td>
<td>209.63</td>
<td>63.15</td>
<td>4.75</td>
<td>17.82</td>
<td>12.12</td>
<td>2.68</td>
<td>1.83</td>
<td>5.65</td>
<td>0.85</td>
<td>0.3781</td>
<td>0.1758</td>
</tr>
<tr>
<td>Expected (%)</td>
<td>86.73</td>
<td>5.57</td>
<td>3.79</td>
<td>0.84</td>
<td>0.57</td>
<td>1.77</td>
<td>0.27</td>
<td>0.1182</td>
<td>0.0549</td>
<td>0.1610</td>
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<td>South African coloureds</td>
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</tr>
<tr>
<td>Observed</td>
<td>100</td>
<td>62</td>
<td>18</td>
<td>3</td>
<td>9</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Expected†</td>
<td>99.70</td>
<td>62.41</td>
<td>19.75</td>
<td>1.56</td>
<td>7.11</td>
<td>3.16</td>
<td>1.13</td>
<td>0.50</td>
<td>3.16</td>
<td>0.50</td>
<td>0.2025</td>
<td>0.0400</td>
</tr>
<tr>
<td>Expected (%)</td>
<td>83.72</td>
<td>7.11</td>
<td>3.16</td>
<td>1.13</td>
<td>0.50</td>
<td>3.16</td>
<td>0.50</td>
<td>0.2025</td>
<td>0.0400</td>
<td>0.1800</td>
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<tr>
<td>South African Indians</td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Observed</td>
<td>104</td>
<td>60</td>
<td>41</td>
<td>3</td>
<td>0</td>
<td>0</td>
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<tr>
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<td>104.00</td>
<td>62.31</td>
<td>36.38</td>
<td>5.31</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>South African blacks (Pedi or Northern Sotho)</td>
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</tr>
<tr>
<td>Observed</td>
<td>127</td>
<td>100</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Expected†</td>
<td>126.48</td>
<td>99.65</td>
<td>10.62</td>
<td>0.28</td>
<td>0.88</td>
<td>2.65</td>
<td>0.05</td>
<td>0.19</td>
<td>11.52</td>
<td>0.61</td>
<td>0.0020</td>
<td>0.0177</td>
</tr>
<tr>
<td>Expected (%)</td>
<td>87.05</td>
<td>0.69</td>
<td>2.09</td>
<td>0.04</td>
<td>0.15</td>
<td>9.01</td>
<td>0.48</td>
<td>0.0016</td>
<td>0.0139</td>
<td>0.0092</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Rare variant Pi phenotypes (other than Pi*S- or Pi*Z-) were seen in combination with PiM1- and PiM2-. The differences between the total numbers observed and expected are due to the fact that certain rare, expected phenotypes are not included in the expected totals, i.e. Pi*SVar, Pi*ZVar and PiVar (homozygote).

†This combined sample of South African whites includes 144 healthy controls and 176 breast cancer patients (see text).
samples, except for Indians, where all individuals studied were found to be of this phenotype. The severely deficient Pi phenotypes, i.e. the two homozygotes S and Z and the heterozygote SZ, jointly attain frequencies of about 0.3 - 0.4% in coloureds and whites. In blacks this frequency is very much lower and in Indians no such individuals were seen. In addition to these well-known Pi phenotypes, several rare phenotypes were seen in blacks. It is thought that most of these are due to the Toronto Y variant (in heterozygous combination). This tentative conclusion, however, requires more specific confirmation. The corresponding frequencies of the various Pi allelic genes are listed in Table II. Upon subjecting these data to the conventional Hardy-Weinberg equilibrium test, good agreement between the numbers observed and expected is found; the deviations are statistically non-significant (Table I).

The comparison of frequencies between different population studies depends to some extent on the technique used for the Pi pheno­typing. In the present study the relatively small sample size may entail an additional source of frequency variation, especially for the variant alleles. As demonstrated in Table II, and despite these reservations, the Pi*M (including Pi*M1 and Pi*M2), Pi*S and Pi*Z frequencies of South African whites and coloureds are comparable with those of most European populations. In the Pedi, the Pi*M frequency is lower than recorded for Natal blacks (probably mostly Zulu) (Table II). However, since these authors 16 employed starch gel electrophoresis, which was the method of choice at that time, the difference can very well be due to technical reasons. A recent study on Transvaal blacks 17 gives a Pi*M frequency of 0.927, which is confirmed by the present study. Following this finding it can be seen that the Pi*M frequency of South African blacks is lower than in blacks in the USA and Somalia, and is comparable with frequencies seen in European populations.

### Breast cancer patients

The larger scale study on breast cancer patients was launched because an unexpectedly large number of patients with this condition was found among the first cohort of cases selected for low AAT concentrations (see "Populations, patients and methods"). Among the 176 breast cancer patients screened, the distribution of Pi phenotypes was comparable with that in healthy controls (differences are not statistically significant). Because of this agreement the sample of breast cancer patients is included in an enlarged (combined), white control sample (Tables I and II).

Several previous studies have investigated a possible association between AAT deficiency and different types of malignant tumour. Other authors 16,17 found an increased frequency of hepatocellular carcinoma among PiMZ and PiZZ individuals. A study 17 among South African blacks records no such association and concludes that AAT deficiency does not seem to play an aetiologic role in the manifestation of hepatocellular carcinoma in this population group.

### Patients with low plasma levels of AAT

Among the group of 30 patients, mostly selected for low AAT concentrations and recorded in Table III, 9 PiZZ homozygotes and 10 PiMZ heterozygotes were found. One of them, a boy of 13 years, had presented with severe liver disease and was typed as

<table>
<thead>
<tr>
<th>Population samples (this study)</th>
<th>No.</th>
<th>Pi*M1</th>
<th>Pi*M2</th>
<th>Pi*S</th>
<th>Pi*Z</th>
<th>Pi*Var:</th>
</tr>
</thead>
<tbody>
<tr>
<td>South African whites</td>
<td>144</td>
<td>0.8021</td>
<td>0.1285</td>
<td>0.0417</td>
<td>0.0139</td>
<td>0.0139</td>
</tr>
<tr>
<td>South African white patients</td>
<td>176</td>
<td>0.8153</td>
<td>0.1165</td>
<td>0.0284</td>
<td>0.0313</td>
<td>0.0085</td>
</tr>
<tr>
<td>South African whites combined</td>
<td>320</td>
<td>0.8094</td>
<td>0.1219</td>
<td>0.0344</td>
<td>0.0234</td>
<td>0.0109</td>
</tr>
<tr>
<td>South African coloureds</td>
<td>100</td>
<td>0.7900</td>
<td>0.1250</td>
<td>0.0450</td>
<td>0.0200</td>
<td>0.0200</td>
</tr>
<tr>
<td>South African Indians</td>
<td>104</td>
<td>0.7740</td>
<td>0.2260</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>South African blacks (Pedi or Northern Sotho)</td>
<td>127</td>
<td>0.8858</td>
<td>0.0472</td>
<td>0.0039</td>
<td>0.0118</td>
<td>0.0512</td>
</tr>
</tbody>
</table>

Other population samples:
- Finland 5: 548
- Ireland 5: 1000
- England 5: 926
- Netherlands 5: 1474
- France 5: 1653
- Italy 5: 202
- Italy 5: 500
- Portugal 5: 330
- USA: whites 5: 1933
- USA: blacks 5: 204
- Somalia: Bantu (newborns) 347
- South African blacks (Natal) 16: 226
- South African blacks (Transvaal): 103

1 The Pi*Var allelic genes include several rare, variant Pi alleles (other than Pi*S and Pi*Z) and require specific identification.
2 This combined sample of South African whites includes 144 healthy controls and 176 breast cancer patients (see text).
PiZZ. Liver transplantation was unsuccessful and he died shortly afterwards. The Pi typing of his family is presented elsewhere.\(^1\) Another example was a baby suspected of having galactosaemia. On phenotyping the specific transferase enzyme (GALT), the infant was found to be probably heterozygous for the classic Gt*A deficiency allele (pending confirmatory tests). This in itself is not a sufficient explanation for the marked galactosuria and hepatomegaly in this patient. The subsequent detection of an additional genetic defect, i.e., an underlying PiZZ genotype, however, could very well explain the pathological picture (article in preparation).

**High-risk families**

As stated above PiZZ homozygotes were especially taken as index cases for high-risk families. An attempt was then made to alert the patient to the consequences the specific AAT finding might have for his/her health, for relatives and for subsequent children, and to encourage family members to come forward for Pi phenotyping. In this way it was possible to phenotype 10 family members, most of whom were PiMZ heterozygotes (Table III). In this process a strategy for detecting high-risk families and for prevention was put to the test. In support of this procedure the case of a breast cancer patient found to be PiZZ can be cited. She had suffered from severe discomfort due to poor lung function for many years but had not sought medical advice. Her adult daughter, who complained about similar respiratory problems, was shown to be PiMZ.

**Discussion and conclusions**

The data on South African whites and coloureds (Tables I and II) indicate that some 6-9% may be expected to possess the deficient Pi*S and some 3-5% the deficient Pi*Z alleles. With regard to the severe AAT deficiencies only, PiSZ and PiZZ, about 2-3/1000 whites and coloureds are expected to have these genotypes. These figures are marginally higher than reported for the high-risk populations of Europe.\(^3,4,19\) The implication for preventive medicine and public health is that in South Africa Pi deficiency conditions are of practical importance predominantly in whites and coloureds and much less so in blacks and Indians.

In contrast with treatment, where procedures are either very costly with limited prospects for success (e.g. liver transplantation) or still in an experimental stage (e.g. replacement therapy)\(^3,5,7,21-25\), prospects for prevention appear more promising, practically feasible and cost-effective.\(^4,5,14\)

Prospective studies have shown that about 50% of newborns with PiZZ deficiency will develop biochemical evidence of liver dysfunction in later life, but only 11-30% will present with severe clinical evidence of liver disease, especially during childhood.\(^3,5,7,21-25\) Despite this variability in manifestation and prognosis, it appears that the recurrence risk for severe liver disease within an affected family is very much higher. In fact, it is recorded that 78% (21/27) PiZZ children with liver disease have similarly affected younger, AAT-deficient siblings. This evidence suggests that other familial factors may contribute towards the form and severity of clinical manifestation, and strengthens the case for seeking prenatal diagnosis in a subsequent pregnancy, whenever a previous child with PiZZ deficiency presents with liver disease.\(^26\) Advances in the field of recombinant DNA technology make it possible to determine the Pi genotype of a fetus by directly assaying its AAT genes in fetal cells derived by amniocentesis.\(^27-29\) Individuals with the PiMZ form of AAT deficiency, who constitute about 3-5% of South African whites and coloureds, are at significantly increased risk of cryptogenic cirrhosis of the liver or chronic active hepatitis compared with individuals with normal AAT concentrations.\(^30\)

The majority of PiZZ individuals are expected to develop clinical signs and symptoms of destructive lung disease and emphysema in adult life.\(^5,7,20,24\) As is well known, the eventual manifestation of destructive lung disease is not only determined by the chronic AAT deficiency, but also by inactivation of the AAT molecules by contributory environmental factors such as bouts of inflammation, irritating gases, atmosphere pollutants and cigarette smoke.

The very important contributory effect of cigarette smoke in the manifestation of destructive lung disease has been demonstrated repeatedly and convincingly. If the patient does not stop smoking and avoids polluted atmospheric conditions, AAT deficiency may be compatible with a full lifespan; continued exposure to such environments or to cigarette smoke can result in emphysema and premature death.\(^5,7,13,14,20\) From the viewpoint of prevention, particular importance must also be accorded to PiMZ heterozygotes. Adults of this genotype have about a threefold greater risk than the normal population of developing destructive lung disease and emphysema. Cigarette smoking can again be expected to increase this risk considerably. This increased susceptibility is also borne out by a variety of lung function tests in which higher proportions of PiMZ heterozygotes than normal controls show impaired lung function.\(^4,5\)

Experience derived from this study strengthens the rationale for offering Pi phenotyping as a preventive service, as advocated in other countries.\(^3,5,7,13,14,20\) This can be done by either prophylactically screening asymptomatic at-risk individuals, e.g. those chronically exposed to atmospheric pollutants (such as certain employees in mining and industry), or by diagnosing Pi deficiency phenotypes in patients presenting with cirrhosis of the liver and/or destructive lung disease and then following up and phenotyping the family members of these index cases. Both strategies should be supported by appropriate information and genetic counselling as part of the preventive programme.

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**Table III. No. of Selected Patients/Individuals Typed for Their Pi Phenotypes and Classified According to Indications as Specified**

<table>
<thead>
<tr>
<th>Electrophenetic Pi phenotypes</th>
<th>Lung lesions</th>
<th>Liver lesions</th>
<th>Low plasma levels of AAT</th>
<th>Family members</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>M*+</td>
<td>MS†</td>
<td>MZ†</td>
<td>S</td>
<td>Z</td>
</tr>
<tr>
<td>12</td>
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<td>3</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
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<td>1</td>
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</tr>
<tr>
<td>12</td>
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<td>5</td>
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<td>3</td>
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<tr>
<td>10</td>
<td>3</td>
<td>0</td>
<td>7</td>
<td>0</td>
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<tr>
<td>40</td>
<td>10</td>
<td>2</td>
<td>17</td>
<td>0</td>
<td>9</td>
</tr>
</tbody>
</table>

*Including M1 and M2 homozygotes and M1/M2 heterozygotes.
†The M component is either M1 or M2.

**Indication**

- Low plasma levels of AAT
- Lung lesions
- Liver lesions
- Family members

**Electrophoretic Pi phenotypes**

- M* +The M component is either Mf or M2.
- MS†The M component is either M1 or M2.
- MZ†The M component is either M1 or M2.
- S
- Z
- MVar†The M component is either M1 or M2.
- SVar†The M component is either M1 or M2.

**Discussion and conclusions**

The data on South African whites and coloureds (Tables I and II) indicate that some 6-9% may be expected to possess the deficient Pi*S and some 3-5% the deficient Pi*Z alleles. With regard to the severe AAT deficiencies only, PiSZ and PiZZ, about 2-3/1000 whites and coloureds are expected to have these genotypes. These figures are marginally higher than reported for the high-risk populations of Europe.\(^3,4,19\) The implication for preventive medicine and public health is that in South Africa Pi deficiency conditions are of practical importance predominantly in whites and coloureds and much less so in blacks and Indians.

In contrast with treatment, where procedures are either very costly with limited prospects for success (e.g. liver transplantation) or still in an experimental stage (e.g. replacement therapy)\(^3,5,7,21-25\), prospects for prevention appear more promising, practically feasible and cost-effective.\(^4,5,14\)

Prospective studies have shown that about 50% of newborns with PiZZ deficiency will develop biochemical evidence of liver dysfunction in later life, but only 11-30% will present with severe clinical evidence of liver disease, especially during childhood.\(^3,5,7,21-25\) Despite this variability in manifestation and
The authors wish to thank the Health Department, City Council of Pretoria, for their co-operation with the collection of the blood specimens and the respective doctors and clinics at H. F. Verwoerd Hospital, on some of whose patients Pi phenotypes were performed. A word of special thanks is due to Professor G. Falkson, Department of Cancer Chemotherapy, University of Pretoria, for providing blood specimens from a large sample of breast cancer patients from his clinic and for permitting publication of the Pi data on these patients.

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REFERENCES


Unstable fractures of the thoracic and lumbar spine treated with Harrington distraction instrumentation and sublaminar wires

J.A. LOUW

Summary

Thirty unstable fractures of the thoracic and lumbar spine were treated surgically with Harrington distraction instrumentation supplemented with sublaminar wiring. The angulation was reduced from 26.8° pre-operatively to 4.9° postoperatively, on average. The patients were mobilised and vigorously rehabilitated, starting 10 days after operation, without the support of orthoses or casts, and were followed up for a period of 9 - 30 months postoperatively. The angulation at the last follow-up averaged 5.4°. Five neurologically intact patients remained intact, and 16 patients with initial neurological deficit remained unchanged. All 9 patients with incomplete neurological lesions improved on average through 1.7 grades (Frankel's grading). No neurological deterioration occurred in any patient.

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