HLA and duodenal ulcer

A. ELLIS1, AND J. C. WOODROW

From the Gastroenterology Unit, Broadgreen Hospital, Liverpool and the Department of Medicine, Royal Liverpool Hospital, Liverpool

SUMMARY. One hundred and one white patients, consisting of 78 men and 23 women, with duodenal ulcer were HLA typed. An association was found between duodenal ulcer and HLA–B12.

The aetiology of duodenal ulcer is unknown. That genetic factors play some part has been accepted since the recognition of the familial aggregation of peptic ulcer (Doll and Buch, 1950) and the independent segregation of gastric and duodenal ulcer (Doll and Kellock, 1951). An association between duodenal ulcer, blood group O, and non-secretor status is well established (McConnell, 1966), although less well recognised is the increased frequency of urinary pepsinogen phenotype A and duodenal ulcer (Samloff and Cole, 1975). Polygenic inheritance has been suggested to explain the lack of a simple mode of inheritance (Cowan, 1973).

The possibility of genetic heterogeneity has also to be considered—for example, some families contain individuals with duodenal ulcer, associated with a high serum Gp.I pepsinogen level, this being inherited in an autosomal dominant fashion (Rotter et al., 1976). Furthermore, duodenal ulcer may be associated with gastrinomas in the autosomal dominant multiple endocrine adenomatosis syndrome (Rotter et al., 1977a).

In a recent study of a group of 54 white males, there was reported an increased frequency of the HLA antigen B5 compared with a control group (Rotter et al., 1977b). This present study was carried out to try to confirm this last observation in a larger group of white males and white females.

Methods

One hundred and one white patients were studied, 78 males (age range 19–76 years, mean 44 years) and 23 females (age range 34–67 years, mean 49 years). The majority of the patients were referred for investigation to the Gastroenterology Unit at Broadgreen Hospital, the remainder being seen at the Gastroenterology Unit at Walton Hospital, Liverpool. Duodenal ulcer was diagnosed endoscopically and/or at operation during previous or subsequent surgery. Patients with combined duodenal and prepyloric ulcer were excluded.

HLA typing was carried out for 26 antigens in the A and B series using a modified microlymphocytotoxicity test (Terasaki and McClelland, 1964). The control series consisted of 500 blood donors, medical students, and members of staff from the same geographical area.

Results

The Table shows the frequency of the various HLA antigens in the patients and in controls. The only notable difference between the two series is in respect of HLA B12, which was present in 46·5% of patients and in 29·2% of controls (x²=11·58, p=0·001). As 26 comparisons were made, an approximate correction for this p value is obtained by multiplying by 26 (Svejgaard et al., 1974), giving p=0·026. The relative risk (Haldane, 1955) for B12 positive individuals of developing duodenal ulcer is 2·1, with 95% confidence limits of 1·4–3·3. Of the 78 male patients, 38 were B12 positive (48·7%) and eight were B5 positive (10·3%). Analysis of these results for male patients alone gives results differing very little from the total series.

Sixty-four out of 98 patients with duodenal ulcer who had their ABO blood groups tested were group O positive (65·3%) compared with 48·9% in controls. The frequency of blood group O was not significantly different between B12 positive and B12 negative patients (66% and 64·7% respectively).

Discussion

This study shows what appears to be a significantly increased liability of HLA B12 positive individuals to develop duodenal ulcer with a relative risk of 2·1. A previous study of male Caucasian patients with duodenal ulcer showed an increased risk for B5 but...
no increased risk for B12. The data from the two
studies can be combined by the methods of Woolf
(1955). For B12 the combined relative risk is 1.61
($x^2=6.95$, $p=0.008$) and $p$ for heterogeneity=0.03.
There is thus evidence of the two studies not being
homogeneous in regard to the association with B12.
For B5 the combined risk is 2.0, $x^2=9.22$, $p=0.002$,
and $p$ for heterogeneity=0.08.

In this situation it is important to consider the
possibility that there have been important differences
in the way patients have been selected for study. The
diagnosis of duodenal ulcer in the present study was
based on macroscopical evidence—that is, the ulcer
was seen at endoscopy or surgery. Furthermore,
cases of combined duodenal and gastric ulcer were
excluded because there is evidence that there may be
important differences in aetiology in this group from
that for patients with either duodenal or gastric
ulcer alone (Doll and Kellock, 1951). In addition,
patients on long-term ulcerogenic drugs were also
excluded. Rotter et al. do not state their criteria for
the diagnosis of duodenal ulcer in their patients. It is
important that the way in which patients are ascer-
tained for inclusion in studies of this type is clearly
stated.

The reasons for the differing findings in these two
studies are at present not obvious. Clearly, it would
be useful if additional studies using well-defined
clinical criteria were carried out, the results being
compared and combined with the two studies
analysed here.

We wish to thank all the consultants in the Liverpool
region who have allowed us to use their patients, in
particular Dr R. B. McConnell, Dr R. J. Walker, and
Dr N. Krasner. We are grateful to Mr N. Usher
for technical assistance, to Sister Shaw, Sister
Whibley, and Mrs Walsh who helped in the collection
of specimens, and to Mrs C. McCormack and
Mrs K. Smith for secretarial assistance.

References


of gastric and duodenal ulcers. *Annals of Eugenics, 16*,
231-240.

Haldane, J. B. S. (1955). The estimation and significance of
the logarithm of a ratio of frequencies. *Annals of Human
Genetics, 20*, 309-311.


Rotter, J. I., Gursky, J. M., Samloff, I. M., and Rimoin,
genetic heterogeneity (Abstract). In *Fifth International
Congress of Human Genetics*, edited by S. Armendarias.

Table  HLA antigens in patients and controls

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Duodenal ulcer (101)</th>
<th>Controls (500)*</th>
<th>$x^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive (no.) (%)</td>
<td>Positive (no.) (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>40 39-6</td>
<td>169 33-8</td>
<td>1.25</td>
<td>0.03</td>
</tr>
<tr>
<td>A2</td>
<td>50 49-5</td>
<td>219 43-8</td>
<td>1.11</td>
<td>0.05</td>
</tr>
<tr>
<td>A3</td>
<td>28 27-7</td>
<td>142 28-4</td>
<td>0.02</td>
<td>0.00</td>
</tr>
<tr>
<td>A9</td>
<td>10 9-9</td>
<td>98 19-6</td>
<td>5.36</td>
<td>0.03</td>
</tr>
<tr>
<td>A10</td>
<td>7 6-9</td>
<td>46 9-2</td>
<td>0.54</td>
<td>0.09</td>
</tr>
<tr>
<td>A11</td>
<td>11 10-9</td>
<td>67 13-4</td>
<td>0.47</td>
<td>0.06</td>
</tr>
<tr>
<td>A28</td>
<td>12 11-9</td>
<td>26/451 58-8</td>
<td>0.38</td>
<td>0.14</td>
</tr>
<tr>
<td>A29</td>
<td>12 11-9</td>
<td>33/463 7-1</td>
<td>2.55</td>
<td>0.16</td>
</tr>
<tr>
<td>Aw30/31</td>
<td>2 2-0</td>
<td>25/440 5-7</td>
<td>2.37</td>
<td>0.20</td>
</tr>
<tr>
<td>Aw32</td>
<td>8 7-9</td>
<td>31/458 6-8</td>
<td>0.17</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*In the case of some antigens not all the controls were tested and the relevant numbers involved are given in each instance.
HLA and duodenal ulcer.

A Ellis and J C Woodrow

*Gut* 1979 20: 760-762
doi: 10.1136/gut.20.9.760

Updated information and services can be found at:
http://gut.bmj.com/content/20/9/760

These include:

**Email alerting service**
Receive free email alerts when new articles cite this article.
Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
Stomach and duodenum (1689)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/