Effect of imipramine on the rheumatoid factor titre of psychotic patients with depressive symptomatology

G. G. HAYDU, L. GOLDSCHMIDT, AND A. D. DRYMIOTIS
From The Creedmoor Institute for Psychobiologic Studies, Queens Village, N.Y. 11427, U.S.A.

It was reported by Oreskes, Rosenblatt, Spiera, and Meadow (1968) that patients with depressive symptomatology show a high percentage of elevated rheumatoid factor titre as measured by the sensitized sheep cell test of Heller, Kolodny, Lepow, Jacobson, Rivera, and Marks (1955). They studied the blood samples of patients who were admitted to an acute psychiatric service. We were interested to ascertain whether the antidepressant medication imipramine has any effect on the titre of rheumatoid factor in depressed patients in need of antidepressant therapy. Haydu (1963) suggested that rheumatoid arthritis and depression are sequelae (in mutually exclusive directions) of a predepressive energy constellation that includes a high demand for adenosine triphosphate (ATP). In rheumatoid arthritis, the process was thought to be initiated by a high ATP-ase activity and a relative insufficiency of adrenocortical support. This hypothesis, based on metabolic studies (Haydu and Wolfson, 1950a, b), was responsible for the broaching of chloroquine therapy in 1951 (Haydu, 1951, 1953). Since then there is more direct evidence (Barwick-Schramm and Kołodzieczyk, 1965) that, in rheumatoid arthritis, blood ATP concentrations are low and the levels correlate with the values of seromucoids and alpha-2 and gamma globulins as well as blood sugar curves. There is also more direct evidence that chloroquine inhibits obligatory aerobic ATP production of mitochondria (Arndeser and Heim, 1967; Stell and Thomas, 1972), and that it inhibits ATP-ase activity of the retina (Schmidt and Müller-Limmroth, 1962). According to the above, the study of imipramine effects on rheumatoid factor appeared feasible, especially since it was found (Tarve and Brechtlívá, 1967) that imipramine reduced the activity of brain membrane-bound ATP-ase.

Beyond a double-blind design and a sufficiently long medication period under constant observation, we wished to establish two placebo-controlled observation periods, one preceding and one following the medication period. We also wished to observe patients in need of antidepressant therapy who have been stabilized in a controlled hospital setting (research ward) under an identical environmental and dietary regimen. Rosenblatt, Oreskes, Meadow, and Spiera (1968) found that schizophrenic patients differ significantly as regards rheumatoid factor titres according to whether they had depressive symptomatology or not. These cases of long duration who developed depressive symptomatology then appeared particularly appropriate for our study.

Subjects and methods

Patients were selected according to the following criteria:
(1) They were to be not older than 60 years, and suffering from a chronic schizophrenic process without signs of organicity.
(2) They had to be showing at the time of selection depressive symptomatology which in the opinion of the attending psychiatrist required imipramine therapy.
(3) They had to have no antidepressant therapy at the time of selection and transfer to the research ward.
(4) They had to be free of other illness and of rheumatological history.

They were given a placebo-controlled observation period of 6 weeks' duration followed by 6 weeks of imipramine therapy. The dosage of imipramine therapy was 50 mg. three times a day. The imipramine period was followed by a second placebo-controlled observation period which also lasted 6 weeks. Environmental and dietary conditions remained the same throughout. During the three periods, bi-weekly observations were made of the following determinations:

- Psychiatric interviews.
- Depression scale rating (Zung).
- Approach-avoidance preference test.
- Psychomotor speed test.
- Interaction indices at meals, with visitors, with patients, with nurses.
- Nowlis Affect Check List.
- Complete blood count.
- Serum glutamic pyruvate transaminase.
- Tanned sheep cell agglutination test.

Excepting the last test, all proved non-contributory or showed a non-significant trend. Therefore only the agglutination test will be described here. This followed the method of Heller and others (1955) as modified by Oreskes and others (1968).
Preparation of test sera
Sheep heterophil antibodies were absorbed from test sera by adding to each specimen an equal amount of washed sheep blood cells. The mixture was refrigerated overnight and separated by centrifugation. The observed sera were sheep blood cells. The mixture was refrigerated overnight and then centrifuged, and the tanned cells were washed and then coated through incubation for 30 min. After centrifugation and washing of the coated cells, a titre was run containing tanned sheep cells. Serum specimens were considered agglutination above Oreskes and the third remained unchanged. This confirms the recent observations of Amkraut, Solomon, Allansmith, McClellan, and Rappaport (1973).

Table  Number of patients with positive agglutination at various dilutions in three experimental periods (determinations made bi-weekly)

<table>
<thead>
<tr>
<th>Experimental periods</th>
<th>Dilutions of sensitized sheep cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/40</td>
</tr>
<tr>
<td>Premedication (6 wks)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Medication (6 wks)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Postmedication (6 wks)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>12</td>
<td>11</td>
</tr>
</tbody>
</table>

* Differs from A at the level of 0.001.

Discussion
These results support the view that the antidepressant drug imipramine, while affecting the energy dynamics of depression, reduces the high rheumatoid factor titre...
found in depressed patients. It was somewhat surprising that the change was so prompt. After only 2 weeks the change began to show in most titres. Whether imipramine would reduce the titre of rheumatoid factor in rheumatoid arthritis without depression is an intriguing question. In a preliminary trial, however, we have found that it does.

The reported reduction of cerebral ATP-ase activity by imipramine should not be regarded as a uniform effect. Regional differences may very well be more appropriately related to antidepressant activity than the overall effect. The conformational status of ATP-ase is intimately connected with sulphhydryl bonds and sulphhydryl disulphide interchange. Colloidal gold Regional differences may very well be more effect. penicillamine and appropriately related to inhibitor of rheumatoid arthritis. Chloroquine itself is inhibitors and they have been findings. Some mercurial inhibitors actually increase ATP-ase activity (Weber, 1959; Dreizen and Gershman, 1970) by a different conformational change. This may explain our observation (Haydu, 1956) that Mersalyl uniformly aggravates rheumatoid arthritis. This may also be the reason why inflammatory disease models were affected in a contradictory manner by various thiol group modifiers (Steinetz, Giannina, and Butler, 1973).

Summary

A double-blind, pre- and postmedication placebo-controlled study was made with imipramine in chronic psychotic patients with depressive symptomatology. Both environmental and dietary conditions remained the same throughout. The medication period lasted 6 weeks with 50 mg. imipramine three times a day. The preceding and following observation periods were of the same length. The initial uniformly high rheumatoid factor titres were significantly reduced by imipramine. This reduction continued to a lesser degree into the postmedication period. The results suggest that rheumatoid factor titre and the energy dynamics of depression are related.

References

 BARWIK-SCHRAMP, A., AND KOLODZIEJCZYK, A. (1965) Reumatologia (Warsaw), 3, 111 (The values of adenosinetriphosphate (ATP) in the blood of rheumatic patients)
 —— (1953) Amer. J. med. Sci., 225, 71 (Rheumatoid arthritis therapy: a rationale and the use of chloroquine diphosphate)
 ——, AND WOLFSON, A. H. (1950a) Rheumatism, 6, 9 (Studies on the pathogenesis of rheumatoid arthritis—II)
 ——, —— (1950b) Ibid., 6, 57 (Studies on the pathogenesis of rheumatoid arthritis—II)
 STEINETZ, B., GIANNINA, T., AND BUTLER, M. (1973) J. Pharmacol. exp. Ther., 185, 139 (The role of sulphhydril groups in three models of inflammatory disease)
Effect of imipramine on the rheumatoid factor titre of psychotic patients with depressive symptomatology.

G G Haydu, L Goldschmidt and A D Drymiotis

doi: 10.1136/ard.33.3.273

Updated information and services can be found at:
http://ard.bmj.com/content/33/3/273.citation

**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.

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/