With regard to the action of oral hypoglycaemic drugs, Beutler \(^7\) does not list these either as causing or not causing haemolysis in G6PD-deficient subjects. In a retrospective comparison of elderly male Indian diabetics on meformin or tolbutamide, no difference in reticulocyte counts was found in those with or without G6PD deficiency; such counts were marginally higher than those found in healthy subjects from the same age-sex group. Further, oral hypoglycaemic drugs do not appear to evince a haemolytic reaction in the African G6PD variant; this variant exhibits some 15\%–20% of normal enzyme activity, and drug-induced haemolysis develops only in the face of high drug dosage.\(^2\)

Normal values of HbA\(_1c\) are predicated on an average red cell life span of 120 days; any red cell survival will diminish HbA\(_1c\) formation proportionately for a particular steady state level of serum (plasma) glucose.\(^1,8\) The estimation of HbA\(_1c\) has been advised as a rapid screening test for the evaluation of the degree of haemolytic anaemia, provided diabetes mellitus can be excluded.\(^2\)

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<table>
<thead>
<tr>
<th>UPTIGHT SCORING FOR WOMEN WITH BREAST CANCER AND CONTROL WOMEN MATCHED FOR AGE, RACE, AND SMOKING HISTORY</th>
<th>UPTIGHT scores*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td>ER+ (n = 25)</td>
<td>51±12</td>
</tr>
<tr>
<td>ER- (n = 21)</td>
<td>50±14</td>
</tr>
</tbody>
</table>

*The maximum attainable UPTIGHT score is 40 (ie, correct identification of 40 of 40 odours embedded on scratch-and-smell cards).

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ABnormally Diminished SENSE OF SMELL in WOMEN with Oestrogen Receptor Positive Breast Cancer

SIR,—The pineal gland, its principal hormone (melatonin), and breast cancer are strongly related.\(^3\) Tamarkin et al\(^4\) have described a decreased nocturnal plasma melatonin peak in women with oestrogen receptor (ER) positive breast cancer. Moreover, melatonin inhibits and pinealectomy enhances dimethylbenzanthracene-induced mammary tumours in the rat.\(^5\) Because of the relation between pineal function and sense of smell,\(^6\) we tested olfaction in women with breast cancer and found significantly decreased olfactory function in women with ER positive breast cancer. Both the pineal and olfactory abnormalities may be the result of a potentially correctable neuroendocrine defect.

We used the University of Pennsylvania smell identification test (UPSIT)\(^7\) to evaluate olfactory function in 46 women with breast cancer. The tumours of 25 women were ER+, the remaining 21 tumours being ER-. The extent of disease was stage I or stage II in all but two cases, and none of the women had brain metastases or had received cranial radiotherapy. 4 of the ER+ and 5 of the ER- women had received chemotherapy. The UPSIT scores of the 46 women with breast cancer were compared with the scores of 46 normal controls matched for age, sex, race, and smoking history, factors all known to influence the UPSIT score. The control data were kindly provided by R. Doty and T. Gregor of the University of Pennsylvania Smell and Taste Center.

Women with ER+ breast cancer had significantly reduced UPSIT scores (p<0.01) (table). Women with ER- breast cancer had UPSIT scores that did not differ significantly from those of matched controls (p>0.4). As found by others,\(^8\) women with ER+ tumours were older than women with ER- tumours (p<0.05).

Because of the previously observed melatonin abnormality in ER+ cases, and because melatonin may be a coordinating signal for mammalian reproduction, we investigated the fertility of women with ER+ tumours. There was no significant difference between the fertility of ER+ and ER- women (table).

Perhaps both the pineal and oestrogen abnormalities observed in women with ER+ breast cancer result from a single underlying defect. Since effluent oestroly imparts pass via the median forebrain bundle to the entire lateral extent of the hypothalamus,\(^9\) and since normal mammalian pineal function is dependent on the suprachiasmatic nucleus of the hypothalamus,\(^10\) it is not unreasonable to suggest that both the pineal and oestrogen abnormalities have a hypothalamic origin, possibly the result of a neurotransmitter defect. Indeed, induced hypothalamic lesions increase the incidence of spontaneous mammary tumours in female rats.\(^11\)

If a single neurotransmitter abnormality does underlie the pineal and oestrogen abnormalities, and if this defect can be corrected with a pharmacological agent, a new therapy for ER+ breast cancer may be possible. Equally, if not more important, one can also think in terms of neurotransmitter replacement therapy as a form of breast cancer chemoprevention.

Steven Leher, Eva Levine, William D. Bloomer

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FAMILIAL HUMAN PARVOVIRUS INFECTIONS

SIR,—The human parvovirus (HPV) has lately been incriminated in the astatic crises of patients with chronic haemolytic anaemia\(^1\) and as the cause of erythema infectiosum (fifth disease).\(^2\) We describe here HPV infections in 13 patients in six families, illustrating the different expressions of HPV and its epidemic characteristics. Sera were examined for HPV and anti-HPV total antibodies by counterimmuno-electrophoresis (CIEP) and for specific IgM by antibody capture radioimmunoassay. The results are summarised in the table. HPV was isolated in only one case, specific IgM suggested recent HPV infection in the other twelve. The high incidence of HPV infection in childhood and the interval between the diseases in a family are compatible with previous reports.\(^3\)

HPV astatic crises revealed the familial corpuscular erythroid abnormality in two families.\(^4\) Only one patient, presented simultaneously both astatic crisis and fifth disease; however, patients with chronic haemolytic anaemia do not have erythema

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