

hepatitis virus or viruses which are transmissible by blood.

Additional evidence that an agent other than type-B hepatitis may be transmitted by blood was provided by the report<sup>18</sup> of an outbreak of short-incubation non-B hepatitis and hepatitis-B in southern England associated with the use of three out of four batches of a commercial factor-VIII concentrate. Details of a non-B acute hepatitis outbreak in a hæmodialysis unit in London have also appeared.<sup>19</sup> And, in studies of hepatitis in an endemic zone in Costa Rica, evidence was provided for viral hepatitis other than type A or type B which was not associated with blood-transfusion.<sup>20</sup> In this study E.B. virus and C.M.V. infection were excluded in all but one of the patients.

It is evident from these studies that there is a third and possibly other types of human hepatitis viruses, but there are as yet no precise criteria or specific tests for these agents. The question which now looms large is how to ensure that the current candidate hepatitis vaccines are free of these viruses. It has been suggested<sup>11</sup> that once the biophysical and biochemical properties of a suitable candidate hepatitis-B virus vaccine had been defined and tested for safety and efficacy in susceptible chimpanzees, similar trials in a small number of human subjects should be considered. An issue that may now have to be considered is the similar evaluation and

safety testing of every batch of such vaccines in human subjects, which is clearly undesirable and impractical, until in vitro or animal models become available for the new and as yet unidentified human hepatitis viruses.

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## Occasional Survey

### MENOPAUSAL FLUSHING: DOES OESTROGEN THERAPY MAKE SENSE?

GRAHAM MULLEY

J. R. A. MITCHELL

*Department of Medicine, Nottingham General Hospital, Nottingham NG1 6HA*

IN 1870, 135 conditions were ascribed to the "change of life" including aortic pulsation, hysterical flatulence, blind piles, boils in the seat, pseudo-narcotism, and temporary deafness.<sup>1</sup> The number of symptoms directly attributed to the change of life dwindled as doctors began to realise that because two events occurred at the same time, this did not always imply a causal relation. Indeed, it has proved difficult to ascertain exactly what the true symptoms of the menopause are. Although about 85% of menopausal women have associated symptoms, most of them are able to continue with their normal activities and rarely consult their doctor.<sup>2</sup> The symptoms are subjective and therefore difficult to measure. Moreover, the medical profession has shown little interest in them. For example, Molnar<sup>3</sup> searched *Index Medicus* from 1903 to 1973 under the category of "menopause" for information on hot flushes (or hot flashes as they are known in the U.S.A.) and found only four references.

Many psychological disturbances previously ascribed to the menopause have been shown to be no more common in 45–55-year-old women than in women in other age-groups,<sup>4</sup> and it has been suggested that apart from the obvious changes in menstruation, the only symptoms significantly more common during the menopause are hot flushes and the associated sweats.<sup>5</sup>

Hot flushes are poorly understood and what is known about them can be stated briefly: they predominantly

affect the "blush area" (the central face, neck, and upper chest); they vary considerably in intensity and frequency, affecting some women more than twenty times a day and sometimes continuing for many years; they are said to be worse when the periods stop suddenly, particularly as a result of surgery; and they may be provoked by a warm atmosphere, hot drinks, alcohol, and mental stress. But what are hot flushes? Are they a purely subjective phenomenon or do they have objective manifestations?

In one thorough investigation of a menopausal woman<sup>3</sup> the electrocardiographic (E.C.G.) changes and tachycardia which preceded the subjective feeling of flushing were commented upon. The patient was seen to sweat and the cheeks were felt to be warm, but no mention was made of visible flushing. Molnar states that: "The hot-flash phenomenon is a subjective experience which can occur without noticeable manifestations and can be identified as such only by the person having it." Novak,<sup>6</sup> however, confidently stated that flushes could be seen and counted, but did not specify that he saw them himself. Collett<sup>7</sup> investigated the basal metabolic-rate (B.M.R.) at the menopause in a woman who experienced several flushes during the test. The investigator observed deeper and faster respirations, and an increase in B.M.R. and skin temperature but did not say whether she actually saw flushing. Four women with severe flushing were observed by Hannan.<sup>8</sup> They had palpitations and a feeling of pressure in the head which were abolished as the flush began, and Hannan saw a sudden wave of redness involving the skin of the face and neck which was followed by perspiration over the affected areas. After flushing, the women complained of chills, faintness, and weakness.

Hot flushes, then, may not be purely subjective. The flush can be seen, and the reported associated increased pulse-rate, respiration-rate, skin temperature, B.M.R., and E.C.G. changes could be measured.

What causes hot flushes? Early investigators believed that imbalance of the autonomic nervous system was responsible, but as endocrinology advanced it was assumed that a hormonal disturbance was involved. The mechanism whereby changing hormone concentrations cause flushing has not been satisfactorily explained and the precise nature of "vasomotor instability" remains to be elucidated. Despite the sparse information on the pathophysiology of hot flushes, most contemporary textbooks state confidently that menopausal flushing is either due to reduced concentrations of circulating oestrogens or to an increase in the output of pituitary gonadotrophic hormone. These widely accepted theories, which were called into question over 30 years ago,<sup>9</sup> do not stand close scrutiny.

*That "Vasomotor Instability" is Related to Reduced Concentrations of Circulating Oestrogens*

Ovarian oestrogen production is reduced at the menopause, and in normal women urinary oestrogen concentrations continue to decrease for about 15 years after the cessation of menstruation. The suggested causal relation between declining oestrogen levels and flushing does not explain why:

- (a) Flushes do not occur at all in about 15% of menopausal women.<sup>10</sup>
- (b) There is no chronological relation between the onset of oestrogen deficiency and the onset of flushing. In some women, flushing may precede the irregularity and cessation of periods;<sup>10</sup> after oophorectomy, oestrogen concentrations usually fall long before hot flushes begin.<sup>11</sup>
- (c) There is no correlation between the presence or absence of vasomotor symptoms and the amounts of oestrogen in blood and urine.<sup>12</sup>
- (d) Men and pre-pubertal women do not appear to complain of episodic, spontaneous flushing, although they have low oestrogen concentrations.
- (e) Flushing sometimes occurs in pregnancy when oestrogen concentrations are high.

*That "Vasomotor Instability" is Related to an Increase in Output of Pituitary Gonadotrophic Hormones*

There is an abrupt increase in total urinary gonadotrophins at the menopause, but gonadotrophins are unlikely to be the cause of flushing for the following reasons:

- (a) Gonadotrophin concentrations continue to rise during the 15 years after the menopause, whereas hot flushes progressively decline in frequency, intensity, and duration after the menopause.
- (b) Those menopausal women who have very high concentrations of gonadotrophin are not necessarily the ones with the most troublesome flushes; indeed, an increase in gonadotrophins was observed in menopausal women with no symptoms.<sup>13</sup>
- (c) Hot flushes have been reported to be relieved by oestrogen in doses which have often been too low to inhibit gonadotrophin production.<sup>9</sup>
- (d) Spontaneous flushing is not a feature of other conditions associated with raised gonadotrophin concentrations such as Klinefelter's syndrome.
- (e) Administration of exogenous gonadotrophic agents does not produce flushing.

Thus, no correlation has so far been established between hormonal changes and menopausal flushing and

the rationale for the use of oestrogens to relieve flushing—i.e., that oestrogens replace a deficiency or suppress gonadotrophin production—would not seem to withstand critical scrutiny. Oestrogens may, however, exert their claimed beneficial effect by some direct action on peripheral vessels. As yet there is no evidence to confirm this; indeed, oestrogens may cause vasodilatation.<sup>14</sup> It has been suggested that oestrogens may cause instability of the autonomic nervous system.<sup>15</sup>

The proponents of these theories tacitly assume that the role of oestrogens in the treatment of hot flushes is well established whereas this is not the case.

Ovarian therapy was first used in 1896 at the Landau clinic in Berlin.<sup>6</sup> Some years earlier Murray et al. had produced excellent results by treating thyroid deficiency states with thyroid extract, and an analogy with oestrogenic deficiency in the menopause was postulated. Extracts of ovary or of corpus luteum were used but later these materials were replaced by more refined oestrogen preparations. Initial scepticism was overcome: oestrogens were deemed to be a natural, logical, and effective treatment for menopausal symptoms. There had always been nagging doubts about the carcinogenic effects of oestrogen,<sup>16</sup> but these were soon cast aside.

In 1937 Pratt and Thomas<sup>17</sup> carried out a well-designed double-blind study to compare placebos, barbiturates, and various oestrogens in menopausal women. They remarked on the difficulties inherent in carrying out a trial based entirely on subjective symptoms, but found that the active agents and the placebos were equally successful in relieving hot flushes.

The oestrogen dogma was, however, already firmly entrenched, and this important study was barely commented on in subsequent published reports.

In the succeeding 40 years there have been very few well-conducted double-blind trials of oestrogens in menopausal flushing. A recent study<sup>18</sup> comparing equine oestrogens with placebo found that there were such dramatic clinical improvements in both the treated and control groups that it was difficult to assess the true value of oestrogen therapy.

Despite this dearth of convincing evidence, oestrogens are freely prescribed for menopausal flushing, and the general consensus is reflected by the following statements: "Estrogen lack after the menopause can be associated with vasomotor instability (hot flashes) . . . which are well documented sequelae of a postmenopausal hormone deficiency that can predictably be reversed by replacement therapy"<sup>19</sup> and "There is little dispute that estrogens are effective in modifying menopausal symptoms."<sup>20</sup> We contend that there is no clear-cut relation between hot flushes and oestrogen deficiency and that there is no evidence that oestrogens are significantly better than placebos in treating hot flushes. We suggest that as oestrogens carry a significant risk we should stop prescribing them for a condition which we do not fully understand.

Perhaps we should begin again by investigating the basic mechanism of hot flushing and determining whether any of the objective changes which have been reported to accompany the sensation of flushing can be used to assess the effect of therapy and to reveal the nature of this common but mysterious symptom.

Requests for reprints should be addressed to J.R.A.M.

*References at foot of next column*

## National Health Service

### THE REALLOCATION OF RESOURCES

#### Parallels with Past Experience

KEITH BARNARD

CHRIS HAM

*Nuffield Centre for Health Services Studies,  
University of Leeds*

THE distribution of resources in the National Health Service is unequal, and successive studies have pointed out wide disparities in per-caput expenditure both between and within health regions.<sup>1</sup> As one of the aims of the N.H.S. was to achieve territorial justice in health-care provision, recognition of these disparities led to the appointment, in May, 1975, of the Resource Allocation Working Party, asked to recommend ways of securing a more equitable distribution of revenue and capital allocations. The formula recommended by the working-party for allocating resources to regions has been adopted for the first time in the current financial year, and the problem of how to achieve fairer intra-regional allocations is now being tackled.

The background to the current concern with resource allocation is remarkably similar to that which motivated the Leeds Regional Hospital Board in planning its services as far back as 1950. Having inherited a variety of hospitals in 1948, the board's task was to secure a more rational, equal, and efficient use of services, and in the autumn of 1950 the board had under consideration a plan designed to achieve this. In view of the unequal distribution of beds throughout the region, the plan suggested a reallocation based on standard bed-to-population ratios. It proposed a complex methodology which aimed to equalise opportunities for treatment both between specialties and between areas. And, like the present reallocation plans, the recommendations were prompted by the desire to correct historically determined inequalities.

Surprisingly, it may be thought, the Leeds Board declined to adopt the plan. However, it did so for a number of reasons that have current interest. Firstly, it was argued that the application of uniform bed ratios across the region was misconceived because it failed to recognise that different areas had distinctive needs. In other words, an equal distribution might not be equitable. Following on from this, the second objection was that there was no sense in changing bed allocations if the existing arrangements were reasonably satisfactory. The latter had to be studied carefully to see how well they were working

before modifications were made, otherwise the result might be a change for the worse. Thirdly, the plan's opponents maintained that any reforms had to be implemented incrementally rather than suddenly, to allow time for adjustments in staffing and equipment to be made. Finally, it was argued that the board had to plan by consent, and this meant taking account of public opinion and the attitudes of consultants, and not dictating from above what policy should be.

#### *The Working Party's First Report<sup>2</sup>*

Although the present debate is concerned with allocation of financial resources and the Leeds plan dealt with beds, there are illuminating parallels between the two. In the intervening 26 years noticeable advances have been made in the approach to this problem, and the first interim report of the Resource Allocation Working Party takes cognisance of many of the objections made to the Leeds plan. For instance, although it is subject to further refinement, the formula by which allocations to regions are now made is more sophisticated in that it contains a weighted population factor, and as far as hospital services are concerned takes case-load into account. Overall there is greater emphasis on equity and on opportunity for access to health care of people at equal risk, than on the simpler notion of equality. Again, the working party realistically aims not at perfection but at "less imperfection", and stresses that "a proposal should be accepted only if it can be shown to improve or remedy a defect in the existing system". Lastly, it recognises that the redistribution of resources and the attainment of a more equitable allocation will be a long-term process which will have to be carried out in stages. In any one year, therefore, the redistributive effects will be marginal.

In these respects the current approach to resource allocation represents an improvement on the one put before the Leeds R.H.B. in 1950. On the other hand, a problem which has still to be tackled is how to obtain consent to the reallocation policy, and this was one of the issues which troubled the Leeds Board. Members reacted against the proposal because it seemed to pay insufficient heed to political factors in the shape of public opinion and the views of the medical profession. Much the same can be said of the working party's report, except for the concluding paragraph which includes the following passage: "We cannot emphasise enough that rationalisation of the order envisaged will be illusory unless Ministers are prepared to take a resolute stand when politically sensitive cases or those which are otherwise contested, for example, by CHCs (community health councils), are presented for decision." Yet it is this variable, more than any other, which poses the greatest single threat to the success of the reallocation policy. Thus, the political obstacles to a fairer distribution of resources emerge as an issue which merits more detailed consideration than it has so far been given.

#### *Political Constraints*

Until recently, discussions about how to achieve a reallocation of resources in the N.H.S. centred on the need to bring deprived regions up to the standard of favoured regions. Two years after leaving office, Richard Crossman explained that a Minister who tried to equalise allocations by levelling down would be forced to agree to such steps as ward closures in those regions from which resources were taken. As "no Minister likes to do that", Crossman noted that the only other way of achieving fairer shares was to level up, and he commented: "unless the Health Service budget rises steadily, and unless the percentage of the GNP allotted to it is steadily increased I cannot level up the backward regions to the better regions and the gap remains."<sup>3</sup>

Today, four years after these remarks were made, the proportion of the gross national product allocated to the

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