

## Letter to the Editor

# The Excretion of a Vitamin B6 Metabolite and the Probability of Recurrence of Early Breast Cancer

EILEEN BELL

*Imperial Cancer Research Fund Laboratories, P.O. Box 123, Lincoln's Inn Fields, London WC2A, United Kingdom*

PATIENTS with breast cancer who excrete sub-normal amounts of tryptophan metabolites after a loading dose of 5 g of the amino acid have a greater probability of recurrence of their disease after mastectomy than women with normal or elevated metabolite levels [1, 2]. Since the availability of the co-factor pyridoxal-5-phosphate (PLP) affects the activity of many of the enzymes involved in tryptophan metabolism, we have measured the urinary excretion of the major vitamin B6 metabolite, 4-pyridoxic acid (4-PA) in 79 patients aged 32-72 yr with early breast cancer. The group included 27 with recurrence of the disease and 52, matched as closely as possible for age, stage, menopausal status and date of operation, who had no recurrence. They were chosen by a person unconnected with the work. In the group were 32 pre-menopausal women, 9 menopausal (that is, within 5 yr of their last menstruation) and 38 post-menopausal, 29 of whom had Stage 1 disease and 50 Stage 2. A 24 hr urine specimen was collected during the week preceeding mastectomy and stored at  $-20^{\circ}\text{C}$  until analysed. Urinary 4-PA was determined by the method of Contractor and Shane [3]. Urine specimens from 19 healthy women aged from 32-62 yr were treated in a similar way. They included 8 pre-menopausal women, 4 menopausal and 7 post-menopausal.

The amount of 4-PA excreted by both healthy women and cancer patients varied widely, ranging from 168 to 2500  $\mu\text{g}/24$  hr by the cancer patients (mean 892  $\mu\text{g}$ , S.D.  $\pm 428$   $\mu\text{g}/24$  hr) and from 556 to 2415  $\mu\text{g}/24$  hr (mean 1175  $\mu\text{g}$ , S.D.  $\pm 529$   $\mu\text{g}/24$  hr).

The median amount excreted by the women with breast cancer was 810  $\mu\text{g}/24$  hr. It was found that those patients excreting less than this had a significantly greater pro-

bability of recurrence than those who excreted amounts greater than the median (Fig. 1). (Log-rank test,  $P = < 0.05$ ) [4]. Of those women with Stage 1 disease, 16 excreted amounts greater than the median and 13 less; 22 women with Stage 2 disease excreted more and 28 less than the median amount. Preliminary results show a high correlation between the amounts of 4-PA excreted and those of 3-hydroxy-anthranilic acid (3-HA) ( $r = 0.54$ ,  $P = < 0.001$ ,  $n = 79$ ). Since previous work showed that the excretion of 3-HA following a loading dose of 5 g of L-tryptophan correlated with the probability of recurrence after mastectomy [2], the inference is that endogenous excretion of both 3-HA and 4-PA may also be useful prognostic indicators.

Potera and her colleagues [5] have reported lower than normal levels of plasma PLP in patients with breast cancer but no difference in the excretion of 4-PA between women with breast cancer and normal women. She found in healthy women a mean excretion of  $703 \pm 376$   $\mu\text{g}/24$  hr, in patients with early breast cancer  $678 \pm 224$   $\mu\text{g}/24$  hr, in patients with local metastases  $597 \pm 310$   $\mu\text{g}/24$  hr and with systematic metastases  $671 \pm 256$   $\mu\text{g}/24$  hr. These results indicate that first, the patients in our series with below median levels of 4-PA are likely to have sub-normal levels of plasma PLP, secondly that the metabolism of the compound to 4-PA may be abnormal or that our patients have a low pyridoxine intake. Unfortunately details of their diets are unknown.

The physiological significance of the relationship between low excretion of 4-PA and rapid recurrence is unknown. But if low urinary amounts of 4-PA reflect B6 deficiency, then it might be suggested that there is an impaired immune response in such patients [6, 7] which is associated with so poor a prognosis.

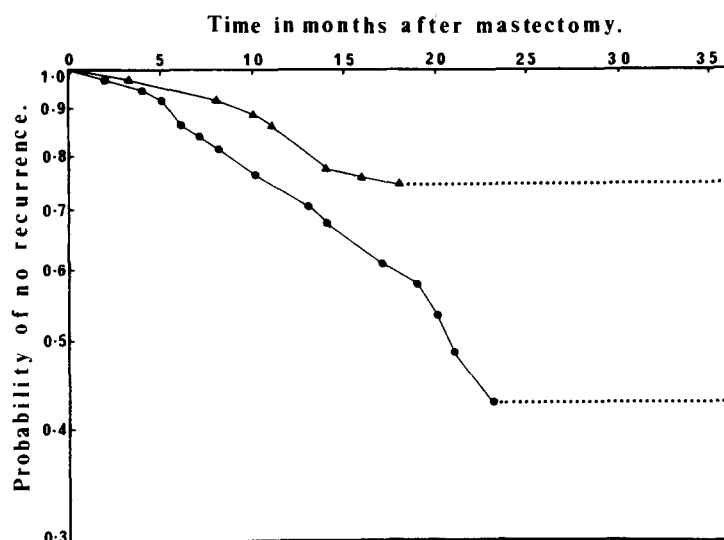


Fig. 1. A comparison between the probability of recurrence after mastectomy in women excreting more than the median amount of 4-PA (closed triangles) and women excreting less than the median amount (closed circles). There were nine recurrences above the median, including two at 8 months and two at 16 months and below the median 18 recurrences (two at 6, 10, 13 and 17 months).

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