use of HRS Mabs in a larger series of patients should permit correlations with ^{67}Ga scanning to be undertaken and the initiation of immunolymphoscintigraphy studies analogous to those achieved in mycosis fungoides with ^{111}In (T101) Mab [8].

The development of specific Mabs in HD and related disorders may provide new insights into diagnostic procedures and new approaches for *ex vitro* (marrow purging) and *in vivo* treatment.

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Growth Factor and Electrolyte Concentration in Human Breast Cyst Fluid

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INTRODUCTION

GROSS CYSTIC DISEASE in women has been shown to be associated with a 2–3-fold increase in the risk of breast cancer [1]. Greater increases in risk have been found in a major subgroup where the benign breast lesions contained atypical hyperplastic changes of the epithelium [2, 3].

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The concentrations of electrolytes in breast cyst fluid (BCF) have been shown to be correlated with the amount of dehydroepiandrosterone sulphate and the pathohistology of the breast [3, 4]. The suggestion is that the latter is related to subsequent breast cancer risk [3].

Recently it has been suggested that growth factors are important in the autocrine or paracrine control of breast carcinogenesis [5]. We have reported on the concentration of insulin-like growth factor-I (IGF-I) and epidermal growth factor (EGF) in BCF [6]. We now extend those results by reporting on their relationship to electrolyte levels in BCF.

MATERIALS AND METHODS

Cyst fluid was obtained by needle aspiration from 80 unselected women attending Guy's Hospital, London, and for whom we have already reported IGF-I and EGF levels [6]. The 41 reported in this paper were obtained on the basis of having had, in addition to IGF-I and EGF, electrolytes measured. The BCF on the 80 subjects were initially obtained to investigate endocrine status especially that of biologically available oestradiol. This assay is methodologically difficult [7] and involved having to perform duplicate assays on an appreciable number of random samples resulting in some samples having too little remaining to perform all three assays. Since the volume of BCF collected for the initial study was similar, any excess being discarded, the subjects studied here were felt to be an unselected group of women with gross cystic disease. The 41 subjects studied comprised 30 premenopausal, five perimenopausal and six postmenopausal women. The average ages (±S.D.) were 47.4 (± 3.2), 51.4 (± 2.9) and 50.8 (± 1.8) years, respectively.

The amounts of IGF-I and EGF in BCF were determined by radioimmunoassay and were as described [6]. The concentration of Na^+ and K^+ were determined by flame emission photometry and Cl^- by coulombmetric titration.

RESULTS

The amounts of Na^+, K^+ and Cl^- were not normally distributed and the median levels of these electrolytes were 61, 94 and 36 nmol/l, respectively. The corresponding ranges were 11–156, 7–198 and <3–110 nmol/l. For all these electrolytes there was an indication of a bimodal distribution. There was 80% of BCF in this study with a N^+/K^+ ratio <3.0 which compares with 70% reported by Boccardo *et al.* [8]. There was a high degree of correlation between the three electrolytes, the regression coefficients being in excess of 0.8.

The levels of IGF-I and EGF in BCF have already been described [6] and both exhibited a non-normal distribution.

There was no significant correlation between the concentrations of IGF-I and any of the electrolytes. This, incidentally, also applied to blood levels of IGF-I. In contrast there was a highly significant correlation between the amounts of EGF and Na^+, K^+ and Cl^- and the ratio Na^+/K^+ (see Table 1). Although the correlations shown have been calculated using non-transformed electrolyte levels, the significance levels were still the same if log-transformed data were used. Further confirmation of the high degree of association between EGF levels and electrolyte concentrations was established by calculating Spearman's non-parametric correlation coefficients for EGF and Na^+, K^+, Cl^- or the ratio Na^+/K^+. These were -0.43 ($P < 0.005$), 0.62 ($P < 0.001$), -0.57 ($P < 0.001$) and -0.48 ($P < 0.002$), respectively.

DISCUSSION

There was a highly significant correlation between the concentration of EGF and the levels of Na^+, K^+ or Cl^- in BCF. This is in keeping with the report of Boccardo *et al.* [8] who found a similar highly significant association between EGF and the ratio Na^+/K^+. Since there is a very highly significant negative correlation between the electrolytes it would be predicted that if EGF is correlated with one electrolyte than the same would follow for the others.

Potentially IGF-I is of great interest since it increases the proliferation of transformed and non-transformed breast cells [9, 10]. Also, the well-described proliferative activity of insulin is mediated through IGF-I receptors [9, 10]. However, although the level of IGF-I in BCF is negatively correlated, albeit weakly, with EGF, there is no correlation between IGF-I and Na^+, K^+ or Cl^-.

One of the striking properties of BCF is the high degree of concordance in the amounts of EGF or IGF-I in multiple cysts, irrespective of whether these were from one or both breasts [6]. Similar comments can be made of electrolytes [11]. Thus the mechanism which controls the type of cyst, and hence the levels of compounds, in BCF appears to be characteristic of the host. Whether these are related to risk of subsequent breast cancer is unknown since at the moment only surrogate measures of risk (e.g. apocrine cell-type) have been used. The only resolution of this would come from a prospective study of patients with gross cystic disease.

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