The even greater inter-individual variations observed in the elderly group make conclusions difficult and indicate that studies on a very large number of subjects might be needed to produce statistically significant data. Nevertheless it appears that older subjects tend to have (a) higher peak levels, (b) later peaks, and (c) 24 h values which are higher than the 12 h mean of the young subjects. Those with the highest peak or 24 h values were not older or lighter than the other members of the group nor did their basic haematology or serum chemistry differ in any way. On the basis of these observations it would seem reasonable to suggest that in some elderly subjects a reduction in dosage and/or once daily administration would be appropriate.

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β -ADRENOCEPTOR BLOCKING AGENTS AND HUMAN FAT CELL ADENYLATE CYCLASE

β -Adrenoceptor blocking agents such as propranolol, alprenolol, prindolol and atenolol are widely used in the treatment of hypertension, heart disease and cardiac dysrhythmias (Shand, 1975; Holland & Kaplan, 1976). Among the side-effects of these compounds is an increase in weight which may occur during treatment (Simpson, 1974; Bengtson, 1972). This weight gain is not caused by fluid retention but possibly is due to the antilipolytic action of these drugs.

Inhibition of fat mobilization is mediated via interaction with the membrane-bound fat cell adenylate cyclase system. An intriguing feature of cyclic AMP mediated lipolysis in adipose tissue is its species specificity. Recently a catecholamine-sensitive adenylate cyclase has been documented in human fat cell ghosts (Kather & Simon, 1976). Noradrenaline and adrenaline (each 0.5 mM) caused a 2–3 fold

increase of cAMP formation. Isoproterenol by inducing an almost 4-fold stimulation of enzyme activity was significantly more potent than the naturally occurring adrenergic agonists.

To assess the usefulness of the human adenylate cyclase system for screening of the antilipolytic activity of β -adrenoceptor blocking agents we compared the effects of propranolol and atenolol on catecholamine-stimulated enzyme activity *in vitro*.

The data presented in Figure 1 show that propranolol as well as atenolol are both effective in inhibiting isoprenaline- adrenaline-stimulated human fat cell adenylate cyclase. However, the concentration of atenolol (1 mM) required to produce half maximal inhibition of isoprenaline- and adrenaline-stimulated enzyme activity exceeded the concentration of propranolol (0.3 μ M) by about three orders of magnitude. The results suggest that atenolol possesses only a slight

Figure 1 Effects of various concentrations of propranolol (●) and atenolol (□) on the isoprenaline (■) and adrenaline (○) stimulated adenylylase of human fat cell ghosts.

Subcutaneous adipose tissue samples were from 5 surgical patients. Fat cells and fat cell ghosts were prepared according to Rodbell (1972). Enzyme activity was assayed according to Salomon, Londos & Rodbell (1974).

Values are given as % of maximal response to the catecholamines. The concentrations of isoprenaline and adrenaline were 0.1 mM and 0.5 mM respectively.

antipolytic activity compared with propranolol in our *in vitro* system. Our data support the contention that weight gain may be lacking or less pronounced during treatment with the 'cardioselective' β -adrenoceptor blocking agent atenolol.

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THE MENSTRUAL CYCLE AND THE TYRAMINE PRESSOR RESPONSE TEST

Variation in autonomic responsiveness during the different phases of the menstrual cycle in women has been reported (Wineman, 1971; Little & Zahn, 1974). In animal studies Wirz-Justice & Lichtsteiner (1976) reported increased noradrenaline (NA) uptake at different areas of the brain in pro-oestrus females than in male rats. We have found sex differences in adrenergic function in human subjects (Ghose, Gifford, Turner & Leighton, 1976). In the intravenous tyramine-dose/pressor response test (Ghose *et al.*, 1976), healthy premenopausal female subjects required less tyramine to increase the systolic blood pressure (BP) by 30 mmHg than did healthy male subjects matched for age. These observations suggested that sex hormones may influence adrenergic function. In order to investigate this further the tyramine pressor response in different phases of the menstrual cycle has been studied.

Five premenopausal female volunteers, aged 23–45 years who were not receiving oral contraceptives or other medication were included in this study. They were physically healthy and had no history of psychiatric illness or gynaecological disorders and their menstrual cycles were regular. During the investigation they were instructed not to take any medication, including hypnotics and analgesics.

Tyramine-dose/pressor response curves were determined by the rapid injection of intravenous tyramine as described previously (Ghose *et al.*, 1976). From the dose response curves the amount of tyramine required to increase the systolic BP by 30 mmHg was determined. This test was performed at the beginning of the week between 10 h 30 min and 13 h 30 min for 4 consecutive weeks. The tyramine-dose/pressor response test which was performed immediately following a menstrual period is