CONCLUSION: A 'field change' in excretion of tumour antigen Cal9-9 occurs in 80% of patients with CRC and rectal mucosal assay of Cal9-9 may be of value in the screening of high risk patients.

206 SEPARATION OF HUMAN PEPSONS IN GASTRIC JUICE BY HIGH PERFORMANCE ION EXCHANGE CHROMATOGRAPHY

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Study of the individual human pepsins is hindered by the absence of a method for their separate quantitation and by the time-consuming methods required for their separation and purification. Using a DEAE 5PW column (TSK, Tokyo, Japan) 7.5 x 0.75 cm, 10 um particle size, with a linear gradient between 0 and 1.0 M NaCl in 0.1 M sodium acetate/acetic acid buffer at pH 4.1 containing 1.0 mM EDTA, and a high pressure ion-exchange chromatography (HPIEC) system, we find that pepsins can be applied to and eluted from the column within 30 min.

Sine pepsin A (Sigma Chemicals, Poole, U.K.) is electrophoretically homogeneous but shows, on HPIEC, two proteolytic components. Pure human pepsin 3 (Roberts, N.B. and Taylor, W.H. Biochem. J. 169, 607, 1978) chromatographs as a single symmetrical peak of proteolytic activity. Purified human pepsin 1 elutes as a series of small unresolved peaks on the ascending limb of a large peak, the descending limb of which is smoothly well-defined. In recovery experiments with human pepsin 3, 100% recovery has been achieved.

Human gastric juice was dialysed against 0.1 M acetate buffer at pH 4.1. After centrifugation the clear supernatant was injected onto the column. Two major symmetrical peaks of proteolytic activity were observed; after elution the larger was shown by electrophoresis to be pepsin 3 and the smaller pepsin 5. In two basal samples of gastric juice the ratio of pepsin 3 to pepsin 5 was 2:1 and 3:1; after pentagastrin the ratios were 5:9:1 during the first 10 min and thereafter 9:1. Pepsin 1, the ulcer-associated pepsin, was not eluted from the column, and requires modified experimental conditions for its quantitation from gastric juice.

At its present stage, HPIEC enables, within 30 min, the ready separation and quantitation of pepsins 3 and 5, which is difficult by conventional chromatography.

207 PHARMACOKINETICS AND DYNAMICS OF INTRAVENOUS INFUSION OF NIFEDIPINE IN A DOSE RANGING STUDY

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There are few pharmacokinetic or dynamic studies of intravenous nifedipine (IV N). IV N might rapidly achieve and maintain steady plasma levels avoiding fluctuations seen after oral administration and allow better control in unstable angina or after acute myocardial infarct. 16 healthy volunteers received N (10mg) in 15% ethanol, 15% polyethylene glycol and 70% water) (13 subjects in 4 groups) or vehicle alone (V) (3) by IV bolus and infusion, in a single blind dose ranging study. Bolus doses of N in each group were: 1) 15 ug/kg; 2) 20 ug/kg; 3) 25 (3); 4) 25 (3). Infusion doses were: 1) 10 ug/min x 8 hrs; 2) 15 x 8 hrs; 3) 20 x 8 hrs; 4) 25 x 4 hrs, 30 x 4 hrs. 3 further subjects received V in a dose equivalent to group 3.

Mean blood pressure (MBP), heart rate (HR) and forearm blood flow (FBF) were measured non invasively. Serial blood samples were taken for N plasma levels. Statistical analysis was by analysis of variance and Student's t test. Haemodynamic changes (mean ± SEM) after bolus were:

Grp HR(beat/min) MBP(mmHg) FBF(%change)
1 *+10 ± 2* -3 ± 3 -23 ± 5
2 -7 ± 2** -9 ± 3* -35 ± 27
3 *+14 ± 4** -2 ± 3 +6 ± 26
4 *+17 ± 4** -8 ± 2* +54 ± 18**

V reduced MBP (-3 ± 9) and FBF (-20 ± 15) and increased HR slightly (5 ± 2). There were no sustained haemodynamic changes on prolonged infusion. N level at steady state in each group was: 1) 13.4 ± 0.3 ng/ml; 2) 17.1 ± 1.0; 3) 18.0 ± 2.0; 4) 35.7 ± 2.7. Mean clearance was 0.89 ± 0.08 l/min, volume of distribution 2.26 ± 0.37 l/kg and half life 1.66 ± 0.19 hrs. Pharmacokinetics results were similar to other N prepaations and showed no significant differences between the groups. Side effects included headache and lethargy (7 of N), flushing (3 of N) and thrombophlebitis (1 of N). Further study of V alone is required.* P < 0.05; ** P < 0.01 compared to baseline; P < 0.01 compared to V

208 COMBINED VASODILATION AND B-ADRENERGIC BLOCKADE THERAPY IN PORTAL HYPERTENSION

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While B-blockade with propranolol (PROP) or vaso dilation with glyceryl trinitrate (GTN) may reduce portal venous pressure (PVP) the effect of both combined has not been studied. In six patients (2 male, 4 female) mean age 57 with histologically proven alcoholic cirrhosis PVP and liver blood flow (LBF) were estimated from the portal hepatic venous gradient during hepatic vein catheterisation and the rate of systemic clearance of indocyanine green (ICG) to its hepatic extraction. PVP, LBF, mean arterial blood pressure (MAP) and heart rate were measured prior to (Control) and following intravenous administration of (a) GTN 500 μg over 20 min, and following return of pressures