

to the disease factor, to tissue response, and to drug delivery at the target site.

May I suggest that the problem is further complicated by that fourth dimension, time? By that I mean the time of administration in relation to the subject's biological rhythm. There is a definite variability in drug utilization according to the phase of the individual diurnal cycle. Plasma levels would therefore be even more helpful if they could be related to the patient's daily rhythm.—I am, etc.,

KLAUS HEYMANN

London W.11

More about D and V

SIR,—Acute transient attacks of diarrhoea and vomiting are so common in general practice that it would be surprising if there were no precise figures for their incidence, and it is perhaps a little misleading to suggest (leading article, 5 October, p. 1) that information is lacking on this side of the Atlantic.

The symptom complex is not always easy to define, but intestinal infectious disease, including food poisoning, dysentery, enteritis, and diarrhoea, has been notified weekly to the Birmingham Research Unit of the Royal College of General Practitioners since 1965. Data from 40 reporting practices are thus available for examination for seasonal and other trends. Further information on the incidence and prevalence of intestinal infections (I.C.D. 003-009) and acute vomiting and diarrhoea (I.C.D. 784.1) is derived from routine analyses of diagnostic indexes maintained in research practices throughout the country.

The most up-to-date figures for episodes of illness under the above rubrics are in the first report of the second National Morbidity Survey¹ carried out by the Royal College of General Practitioners, the Office of Population Censuses and Surveys, and the Department of Health and Social Security. Every relevant episode occurring in one year in over 50 practices was recorded. Taking the two rubrics together there were 51.7 episodes of illness per 1,000 population as against 260.2 episodes of disease of the upper respiratory tract. Episodes occurred most often in northern England and in Wales.

The nature and cause of "D and V" has not been overlooked by general practitioners in Britain^{2,3} and Australia,⁴ and others have been concerned with its treatment.⁵⁻⁷ Epidemic winter vomiting came under scrutiny both by individuals and by the Epidemic Observation Unit of the Royal College of General Practitioners⁸ as far back as the 1950s.

What are the implications of observations in general practice for others who seek to discover possible causes? That "D and V" affects travellers overseas and that it often occurs when patients move from one place to another in Britain is well known. Incidence among new entrants to practices can be observed. Practitioners, too, are aware that exposure to new environmental factors may precipitate episodes in newcomers and they seek to identify ingested factors which may act directly or indirectly by altering the viral status of tissues.

For the moment it may comfort the laboratory worker to know that he may turn to general practice for epidemiological help

and, if he wishes, for sample material from patients with an affliction the existence of which the practitioner has never doubted.—I am, etc.,

R. J. F. H. PINSENT

Research Adviser,
R.C.G.P. General Practice Research Unit
Birmingham

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Further Application of the Nitroblue Tetrazolium Test

SIR,—We note the comments by Drs. A. W. Segal and A. J. Levi (7 September, p. 629) regarding the use of the nitroblue tetrazolium N.B.T. test as an aid to differentiation of lobar pneumonia from pulmonary thromboembolism. While we agree that the frequency of false results diminishes the value of the test in distinguishing bacterial infection from other pyrexial disorders, in our experience there remain certain specific clinical situations in which the technique is of diagnostic assistance. These include chronic granulomatous disease,¹ early detection of bacterial infection in regularly dialysed patients,² and the differentiation of episodes of rejection from infection in renal transplants.^{3,4}

The adoption of strict criteria for the definition of neutrophil N.B.T. positivity has largely overcome observer differences in counting. Our criteria of positivity include: the counting of only those neutrophils with intact membranes; intracytoplasmic formazan deposits must equal or exceed individual neutrophil lobe size; formazan stippling is rated as negative. The use of Ficoll in samples anticoagulated by EDTA minimizes cell clumping and membrane disruption.⁵

We agree that raised N.B.T. results occur following myocardial infarction⁶ and surgical operation.⁷ This was very much in our minds in our own series (3 August, p. 317). The reference by Drs. Segal and Levi to "a group of patients, most of whom were postoperative or post-partum with pulmonary thromboembolism" is inaccurate. One patient had undergone minor surgery seven days prior to the development of the embolic incident. One patient developed pulmonary thromboembolism five days following myocardial infarction. In both instances the diagnosis of pulmonary thromboembolism was angiographically proved. No post-partum patient was included in our series. We note their comments regarding the validity of this trial. We do not consider, however, that this is a situation in which control in the usual sense can be applied.

We agree that the initial enthusiasm for this test as an indication of bacterial infection has not been fulfilled.^{8,9} We do, however, maintain the view that the N.B.T. test provides useful ancillary information in the

context of pulmonary thromboembolism versus lobar pneumonia.—We are, etc.,

R. M. ROWAN

A. M. GORDON

A. K. R. CHAUDHURI

FRANCIS MORAN

Department of Haematology,
Royal Infirmary,
Glasgow

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Transthoracic Electrical Impedance in High-altitude Hypoxia

SIR,—In their interesting article on high-altitude pulmonary oedema (28 September, p. 771) Professor S. B. Roy and others found a consistent increase in transthoracic electrical impedance while clinical improvement occurred.

They felt that this "decrease in impedance values could not be correlated objectively with increased thoracic fluid volume as shown by changes in pulmonary blood volume or pulmonary extravascular space." There must, however, be little doubt that thoracic fluid volume does decrease with clinical improvement, as in his report of 101 cases of high-altitude pulmonary oedema followed radiologically Menon¹ found progressive clearing of the lung fields with treatment in the 97 patients with a successful outcome.—I am, etc.,

R. M. ELLIS

Charing Cross Hospital (Fulham),
London W.6

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False Positive Pregnancy Test in Uraemia

SIR,—We would like to record two cases of uraemia which presented with clinical features suggestive of a septic incomplete abortion. The Gravindex pregnancy test gave a positive result which on further study proved to be a false positive result. Details of the two cases are as follows.

The first patient, an African woman aged 33 years, was admitted with a history of headache, weakness, and malaise for four days. Physical examination revealed an ill, toxic, pyrexial patient. There was pallor of the mucous membranes with mild icterus. The blood pressure was 180/120 mm Hg, and the apex beat in the sixth interspace outside the midclavicular line and heaving in character. Bilateral basal crepitations were present. Soft exudates present in the optic fundi. Other systems were normal. Investigations: urine contained a trace of albumin and more than 10,000 *Escherichia coli*/ml, blood urea 130 mg/100 ml, serum sodium 135 mEq/L, serum potassium 2.9 mEq/L, serum chloride 93 mEq/L, CO₂ combining content 14.1 mEq/L, serum bilirubin 3 mg/100 ml, serum alkaline phosphatase 4 KA units, serum albumin 3.6 g/100 ml, serum globulin 4.7 g/100 ml, blood sugar 115 mg/100 ml, serum creatinine 6.5 mg/100 ml. The Gravindex pregnancy test was positive on three occasions and on the last occasion the quantitative test was positive at a level of 7,000 IU/l. A chest x-ray showed cardiomegaly with congested lung fields.