removes all clothing from above the waist. Most of us find it difficult enough to examine the jugular venous pulse, for example, without the added encumbrance of a "pulled-up nightie", acting like a scarf round the patient's neck.

Surely the point that Dr Wright is making is that one should perform as dignified and thorough examination in an elderly person as one would in any other patient.

16 Angells Meadow,
Ashwell,
Baldock, Herts. D. ROWLEY JONES

RADIOIMMUNOASSAY FOR NORTRIPTYLINE AND AMITRYPTYLINE

SIR,—Dr Aherne and his colleagues (June 4, p. 1214) correctly draw attention to the advantages of their radioimmunoassay (R.I.A.) for estimation of plasma concentrations of nortriptyline and amitriptyline in monitoring response of patients receiving these drugs. However, a wide range of monoamine-reuptake-inhibiting drugs is now used in treatment of depressive illness, and an advantage of some other analytical methods, such as the gas-liquid chromatography method described by Gifford et al.,[1] is that they can readily estimate most of these drugs and their main metabolites[2] as well as identify some other centrally acting drugs such as benzodiazepines which the patient may be taking. For example, in a comparative study of two antidepressive drugs, we found that some patients had been given the wrong drug and some were found to be taking benzodiazepines, for part or all of the trial period.[3] Chromatographic and R.I.A. methods both have their analytical roles according to the clinical or research problem being investigated.

Department of Clinical Pharmacology,
St. Bartholomew's Hospital Medical College,
London EC1A 7BE PAUL TURNER

GOALS AND OBJECTIVES IN MEDICAL EDUCATION

SIR,—Your editorial (May 7, p. 985) left me with a profound sense of *déjà vu*. The vocabulary is all too familiar: goals, objectives, facilitation of educational planning, learning activities, feedback. The same jargon has filled many North American medical journals for years. Big business and government in the U.S.A. have long been sending their executives and high-ranking civil servants to management courses that are replete with this type of cliché-ridden claptrap. Instruction in educational methods sounds fine, but I know a person who spent some months at a centre dedicated to such instruction and returned unable to communicate with either his colleagues or his students. As a result, he gave up teaching and became a dean.

You make a not-unreasonable plea that medical students should possess certain basic facts, and cite as an example knowledge of fluid and electrolyte balance. Such a statement reassures me, since for years there has been a popular fallacy that medical students invariably emerge as good and competent doctors despite having been educated in a factless vacuum. But elsewhere, the trend is for no set curriculum, no examinations, two basic facts, one anatomical and one physiological, and the rest to come about through heuristic osmosis. This concept of teaching prevails at one well-known Canadian medical school, a school whose pedagogic methods have repeatedly been featured as the ne plus ultra in both *The Lancet* and the *British Medical Journal*.

The problem of how and what to teach, and for what purpose, is general, and afflicts not only medical schools but all institutions of learning. It is unlikely to be brought under control by random and capricious changes of curricula, by lowering of standards, by getting rid of written examinations, or by holding conferences in medical education and publishing the proceedings in an ever-proliferating jargon. Goals and objectives are all very well, but those who teach in and administer institutions of learning might do well to recall how Sydney Smith defined the purpose of education: "to give children resources that will endure as long as life endures; habits that will ameliorate, not destroy; occupations that will render sickness tolerable, solitude pleasant, age venerable, life more dignified and useful and therefore death less terrible."

Department of Medicine,
School of Medicine,
West Virginia University,
Morgantown, West Virginia 26506, U.S.A. W. KEITH C. MORGAN

MAXIMAL ACID OUTPUT AND RISK OF ULCER

SIR,—Our articles[1-3] have provoked criticisms from those, notably Dr Sircus[4] and Dr Prescott[5], who cherish the belief that duodenal and gastric ulcers are different diseases. In support of this belief Dr Sircus cites the presence of gastritis in gastric ulceration but overlooks its presence in duodenal ulceration.[6] He regards pyloric reflux as a feature of gastric ulceration but overlooks its presence in duodenal ulceration especially when measured 30 minutes after infusing acid into the duodenum.[7,8] He mentions gastric stasis as a possible ætiological factor in gastric ulceration but ignores the evidence showing that the rate of gastric emptying is rarely delayed and may even be increased in patients with gastric ulceration.[9,10] He suggests that stasis may be a factor in the pathogenesis of the gastric ulcers which follow vagotomy and drainage for duodenal ulceration but ignores the fact that both the incidence of recurrent G.U.S and the rate of gastric emptying increase as the capacity to secrete acid after vagotomy decreases.[1,11] In addition to his disregarding these many facts Dr Sircus misquotes our paper, claiming that we had a preposterous 21·2% incidence of recurrent ulcers when in fact we clearly state that our incidence was 7·8%.

Despite these criticisms Dr Sircus concedes that the deduction, that the capacity to secrete acid increases with increasing duration of symptoms, is consistent with his earlier observations. Standardisation of secretory data for age or lean body mass, or more appropriately for height,[12] is necessary before the relationship between M.A.O. and duration of symptoms can be demonstrated in retrospective studies. Appropriate standardisation of secretory data should therefore be achieved before the data from retrospective studies, such as those of Petrillo et al.[13] can be accepted as evidence against the existence of such a relationship.

Dr Sircus draws attention to the unusually large proportion of low secretors in our control subjects. This unusually large proportion of low secretors may reflect the relatively poor

1. Gifford, L. A., Turner, P., Pare, C. M. B. *J. Chromatogr.* 1975, **105**, 107.
2. Witts, D., Turner, P. *Br. J. clin. Pharmac.* 1977, **4**, 249.
3. Witts, D., Turner, P., Mulgirigama, D., Pare, C. M. B. *Postgrad. med. J.* (in the press).

1. Fiddian-Green, R. G., Bank, S., Marks, I. N., Louw, J. H. *Lancet*, 1976, ii, 1367.
2. Fiddian-Green, R. G., Bank, S., Marks, I. N., Louw, J. H. *ibid.* p. 1370.
3. Fiddian-Green, R. G. *ibid.* 1977, i, 74.
4. Sircus, W. *ibid.* p. 594.
5. Prescott, R. J. *ibid.* p. 595.
6. Magnus, H. A. *in* Modern Trends in Gastroenterology (edited by F. Avery Jones). London, 1952.
7. Fiddian-Green, R. G., Russell, R. C. G., Hobsley, M. *Br. J. Surg.* 1973, **60**, 322.
8. Wormsley, K. G. *Gut.* 1972, **13**, 243.
9. Capper, W. M. *Ann. R. Coll. Surg. Engl.* 1967, **40**, 21.
10. Faber, R. G., Maybury, N. K., Ralphs, D. N. L., Hobsley, M. *Gut*, 1976, **17**, 829.
11. Thompson, J. P. S., Russell, R. C. G., Hobsley, M., Le Quesne, L. P. *ibid* 1974, **15**, 200
12. Hobsley, M., Whitfield, P. F., Faber, R. G., Parkin, J. V., *Lancet*, 1975, ii, 101.

RISK OF ULCERATION EXPRESSED AS PERCENTAGE/10 YEARS IN SUBJECTS WITH EQUIVALENT CAPACITIES TO SECRETE ACID

Percentage risk in "normals" and post-vagotomy patients computed on the assumption that 1·7% of all normal individuals and 7·8% of all post-vagotomy patients develops an ulcer in 10 years.[1] (Patients with M.A.O. >40 meq/l have been included in this table.)

Maximum acid output (meq/h)	"Normals"			Students			V + D			V+A		
	No.	U	%	No.	U	%	No.	RU	%	No.	U	%
0–5	154	103	0·5	7	0	0	89	13	5·4	20	1	1·5
5–10	102	116	0·8				57	14	9·0	34		
10–15	99	174	1·3	32	0	0	48	6	4·6	11		
15–20	96	195	1·5				26	7	9·9			
0–20			0·9			0			6·7			1·5
20–25	57	211	2·6	58	1	1·7	24	11	16·8	0	0	0
25–30	36	168	3·3				19	6	11·6	0	0	0
30–35	19	161	6·1	36	1	2·8	9	1	4·1	0	0	0
35–40	14	115	5·9				8	3	13·8	0	0	0

V + D: vagotomy and drainage
V + A: vagotomy and antrectomy
U=ulcer
RU=recurrent ulcer

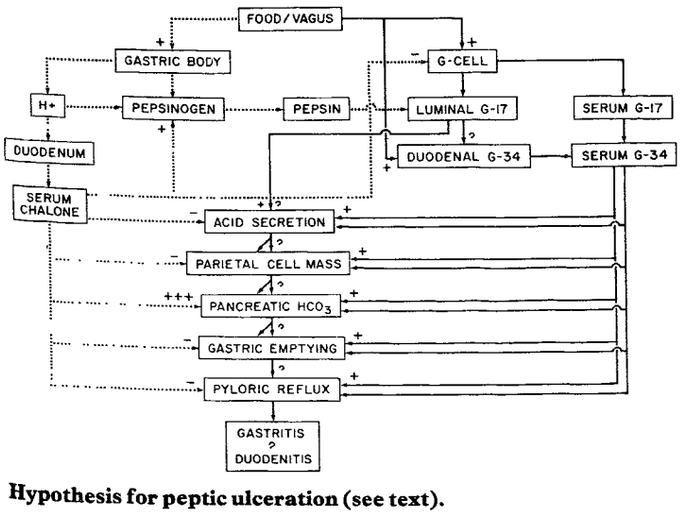
nutritional state and the relatively large incidence of nutritional anæmia in the Cape Town population. Despite this apparent skewness in the distribution of our control population, our incidence of hypersecretion corresponds more closely with those observed in other centres than does that observed by Dr Sircus.[12,14] Unfortunately the true limits of normality in Cape Town, or in any other community, are not known, for the appropriately designed prospective control studies have not been performed. Accordingly the evidence which is cited in support of the hypothesis, that hypersecretion precedes the development of ulcers, is in Fordtran's words, "hardly conclusive".[14]

Both Dr Sircus and Dr Prescott question the validity of the conclusions in our paper on the M.A.O. and risk of ulceration on statistical grounds. Such criticism is inappropriate for the retrospective nature of the study, the incomplete follow-up, and the assumptions that we had to make in order to calculate the risks of ulceration prevented us from using statistical comparisons to support our conclusions. Unfortunately it is most unlikely that a prospective study of sufficient magnitude to test the validity of our conclusions or of the views of Dr Sircus and Dr Prescott will ever be performed. Fig. 3 and the succeeding figures, to which Dr Prescott refers were derived from values obtained from the regression equation between the M.A.O. and the incidence of recurrent ulcers. The points, which these figures were intended to portray, are emphasised in the accompanying table which includes details of the patients treated by vagotomy and antrectomy. The table shows the striking difference between the calculated risk of recurrence following vagotomy and drainage and the calculated risk of ulceration in normal individuals with the same M.A.O. The difference is consistent with the deduction that ulcers are not caused by an abnormal capacity to secrete acid and does not support the deduction that ulcers are caused by an abnormal capacity to secrete acid. The similarity between the M.A.O. in our post-vagotomy subjects and the M.A.O. in patients with recurrent duodenal or gastric ulcers, to which Dr Sircus refers, further supports the deduction that ulcers are not caused by abnormal capacity to secrete acid.

Acknowledging the fact that duodenal ulcers may develop in patients who have a normal capacity to secrete acid, Dr Sircus suggests that ulcers may be caused by the inappropriate secretion of acid that has been demonstrated in patients with duodenal ulcers. This may be so, but, in the absence of data from similar experiments in patients with gastric ulcers, this evidence cannot be accepted as support for the belief that duodenal and gastric ulcers are different diseases. The accompanying table illustrates the striking similarity between the actual incidence of recurrence following vagotomy and antrectomy and the calculated incidence of ulceration in normal individuals with the same capacity to secrete acid. These data form the basis for our deduction that antrectomy tends to cure patients of their ulcer disease. Dr Sircus questions this deduction on the grounds that a Billroth-I antrectomy is ineffective treatment for duodenal ulceration but overlooks the evidence that Billroth-I antrectomy is effective treatment for duodenal ulceration provided that sufficient antrum is removed.[15,16] Even so, in terms of the hypothesis I presented,[3] a gastrojejunal anastomosis does have a theoretical advantage over a gastroduodenal anastomosis for it impairs the release of duodenal gastrin by food. The impairment may account for the relative success of gastrojejunostomy in the treatment of duodenal ulceration. How does Dr Sircus account for a therapeutic success of a gastrojejunostomy?

The hypothesis I proposed is illustrated in the accompanying figure. All the abnormalities which have been described in peptic ulceration can be explained by postulating that the release of chalone is impaired and that ulcers form in areas that are primarily determined by each individuals capacity to secrete acid. As Schaffalitzky de Muckadell et al.[17] observed it may not be possible to demonstrate an impaired release of secretin in peptic ulceration by perfusing acid into the duodenum. In most instances the abnormal responses to

13. Petrillo, M., Grossi, E., Porro, G. B. *ibid.* 1977, i, 596.
14. Fordtran, J. S. *in* Gastrointestinal Disease (edited by M. H. Sleisenger and J. S. Fordtran); p. 174. Philadelphia, 1973.



Hypothesis for peptic ulceration (see text).

15. Nyhus, L. M., Harkins, E. Surgery of the Stomach and Duodenum, p. 258. Philadelphia, 1969.
16. Stempien, S. J., Lee, E. R., Dagradi, A. E. *Surgery*, 1972, **71**, 110.
17. Schaffalitzky de Muckadell, O. B., Fahrenkrug, J., Stadil, F. *Lancet*, 1977, i, 596.

duodenal acidification, to which I have referred in my hypothesis, have been observed in response to pharmacological amounts of acid. The pathophysiological significance of an abnormal response induced by a pharmacological stimulus may be questioned but it is well established that provocative stimuli are sometimes necessary to demonstrate hormonal abnormalities in other endocrine disorders. As indicated in my hypothesis, the abnormal release of secretin may only be part of the abnormal response to duodenal acidification. It is perhaps more appropriate to refer to the hormone or hormones, whose release appears to be impaired in peptic ulceration, as chalones. In looking for a chalone whose release is impaired in peptic ulceration we should not overlook the possibility that an impaired release may be manifest as an impairment of basal release rather than of stimulated release. Furthermore we should not overlook the possibility that basal concentrations of immunoreactive chalone may not reflect the biological activity of the chalone in its basal state.

Department of Surgery,
University of Michigan,
General Surgical Associates,
1405 East Ann Street,
Ann Arbor,
Michigan 48109, U.S.A. RICHARD G. FIDDIAN-GREEN

SIR,—We were fascinated, and rather perplexed, by Dr Fiddian-Green's interpretation and statistical treatment of our acid secretory data.[1-3] His views have perturbed some of our colleagues[4] who, like ourselves, have championed the view that acid-pepsin aggression is a major ætiological factor in duodenal ulcer, and impaired mucosal resistance an important cause of gastric ulcer. However, fundamental similarities between gastric and duodenal ulcers have also been noted[5-8] and recent complicated statistical studies by Hobsley et al.[9] have purported to show that duodenal ulceration is the cause, rather than the result, of acid hypersecretion. Dr Fiddian-Green can hardly be blamed for choosing to extend this concept by examining our data for evidence of similarities, rather than differences, in the pathogenesis of peptic ulcers. In this respect, many of the current views on the pathophysiology of peptic ulceration require almost as much "further study" as do those of Dr Fiddian-Green. Guth[10] believes that the role of antral gastritis and bile reflux in gastric ulceration is suggestive rather than proven, and studies showing increased parietal-cell sensitivity to gastrin in duodenal ulceration[11] and, indeed, other findings on hormonal and homœostatic differences between duodenal-ulcer and control subjects do not exclude the possibility that the same may apply to gastric or, at least, prepyloric ulceration. Dr Fiddian-Green's unitarian hypothesis is in keeping with the suggestion that gastric ulcers be regarded as duodenal ulcers in the wrong place,[12] and his evidence that the acid secretory capacity of the stomach influences the position in which an ulcer may develop gives statistical expression to the time-honoured concept of the gradient of mucosal vulnerability to peptic ulceration.[6]

It is unfortunate that many workers draw conclusions from conventional and, it seems, questionable statistical correlations[13] which lean heavily on acid secretory data standardised for either height, weight, lean body mass (L.B.M.), or age. Significant correlations, usually with lower values, have been shown to exist between the M.A.O. and one or more of these measures in control subjects,[9,14-17] but the correlation between M.A.O. and body habitus in D.U. patients is more tenuous.[9,15,16,18] To date, there is no consensus about which of the indices of body habitus offer the best correlation with M.A.O.[16,17] Hassan and Hobsley[16] found that L.B.M. offered the better correlation with acid secretion "corrected for pyloric loss", whereas Novis et al.[17] noted that the correlation between body weight and M.A.O. was slightly better than that between M.A.O. and L.B.M. in a large group of students of relatively uniform age. In any event, Hobsley et al.[9] "corrected" their secretory data for height, Fiddian-Green et al. calculated age-standardised acid outputs, and Sircus[4,19] simply expressed his data in terms of acid output per kg body-weight. Dr Fiddian-Green is clearly in good company, although we must concede that his use of age-standardised M.A.O.s in correlating M.A.O. with duration of symptoms was perhaps unwise.

Dr Sircus's comments are, in the main, well taken, but it is only fair that we, too, should be confused by his data pertaining to the possible influence of duration of symptoms on M.A.O. The data on his 200 D.U. patients in the table[4] suggest that the mean M.A.O., expressed in mmol/kg T.B.W./h, remains constant irrespective of the duration of symptoms. This is in striking contrast not only to his earlier findings[20] in 176 D.U. patients where M.A.O. was expressed in meq/h but also to his later study[19] on 339 patients in which M.A.O. was expressed in mmol/kg T.B.W./h. This study, interestingly enough, showed that the M.A.O. increased progressively with duration, that there was no "fall-off" in M.A.O. in the groups of patients with symptoms of more than 19 years' duration, and that the progressive and significant increases in M.A.O. with duration applied equally to "normosecretor" and "hypersecretor" type of D.U. patients.

Perspective regarding the influence of duration on M.A.O. in D.U. patients and its pathophysiological implications may perhaps be gained from data from a study carried out some 20 years ago in 63 D.U. patients with no clinical, radiological, or surgical evidence of stenosis.[18] No significant correlation was found between M.H.R. (maximal histamine response expressed in meq/30 minutes) and duration of symptoms for the entire group of 63 patients, but a significant positive linear correlation between M.H.R. and duration was found in the subgroup of 49 patients with a history of up to 12 years' duration ($r=0{\cdot}305$, $P<0{\cdot}05$). A multiple regression of M.H.R. on body-weight, age, and duration in this subgroup was also found to be significant ($r=0{\cdot}31$, $P<0{\cdot}05$) but the "beta" correlation coefficients left little doubt that only duration had a significant influence on M.H.R. ($P<0{\cdot}05$). It should be stressed that only about 10% (i.e., $0{\cdot}31^2 \times 100$) of the total variance in the M.H.R. was associated with variances of duration. Further statistical scrutiny of the data in the entire group of 63 D.U. patients, including the 14 with a duration of more than 12 years, showed that the correlation between M.H.R. and duration could be better fitted to a curvilinear ($P<0{\cdot}01$) than to a linear regression. However, only 22% of the total variation in M.H.R. could be accounted for by consideration of sex and the quadratic and linear terms for duration. Age and body-weight again showed no significant contribution to the regression. The data, while supporting the contention that the M.H.R. tends to increase with duration in D.U. patients,[2,9,16] emphasises the point that factors other than duration, sex, and the negligible effects of body-weight and age are responsible for the magnitude of the M.H.R. in the vast majority of duodenal-ulcer patients, and

1. Fiddian-Green, R. G., Bank, S., Marks, I. N., Louw, J. H. *Lancet*, 1976, ii, 1367.
2. Fiddian-Green, R. G., Bank, S., Marks, I. N., Louw, J. H. *ibid.* p. 1370.
3. Fiddian-Green, R. G. *ibid.* 1977, i, 74.
4. Sircus, W. *ibid.* p. 594.
5. Hurst, A. F., Venables, J. F. *Guys Hosp. Rep.* 1929, **79**, 249.
6. Card, W. I., Bruce, J., British Surgical Progress. p. 15. London, 1959.
7. Shay, H. *Rev. Brasil. Gastroent.* 1954, **6**, 801.
8. Marks, I. N., Shay, H. *Lancet*, 1959, i, 1107.
9. Hobsley, M., Whitfield, P. F., Faber, R. G., Parkin, J. V. *ibid.* 1975, ii, 101.
10. Grossman, M. I., Guth, P. H., Isenberg, J. I., Passaro, E. P., Roth, B. E., Sturdevant, R. A. L., Walsh, J. H. *Ann. intern. Med.* 1976, **84**, 57.
11. Isenberg, J. I., Grossman, M. I., Maxwell, V., Walsh, J. H. *J. clin. Invest.* 1975, **55**, 330.
12. Illingworth, C. Personal communication.
13. Prescott, R. J. *Lancet*, 1977, i, 595.
14. Marks, I. N. *Gastroenterology*, 1961, **41**, 599.
15. Baron, J. H. *Gut*, 1969, **10**, 637.
16. Hassan, M. A., Hobsley, M. *Br. J. Surg.* 1971, **58**, 171.
17. Novis, B. H., Marks, I. N., Bank, S., Sloan, A. W. *Gut*, 1973, **14**, 107.
18. Marks, I. N. Unpublished.
19. Larn, S. K., Sircus, W. *Q. Jl Med.* 1975, **44**, 369.
20. Sircus, W., Small, W. P. *Scott. med. J.* 1964, **9**, 453.

suggests that the provocative hypothesis that duodenal ulceration leads to hypersecretion[2,9] applies, at most, to only some 10–20% of such patients.

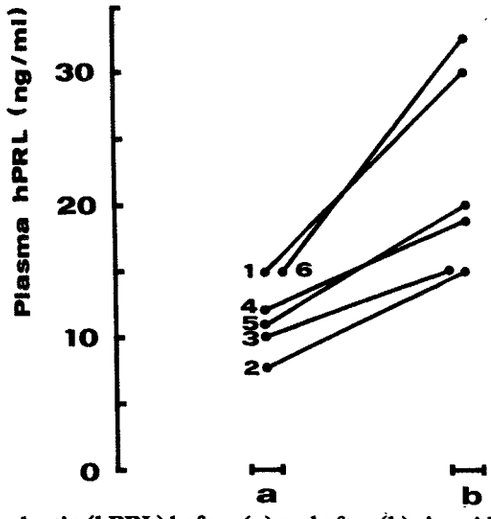
Dr Fiddian-Green's questioning of conventional views on ulcer pathogenesis is not, we believe, a subject for reproach. The reluctant coauthors feel that his avant-garde approach has highlighted the burgeoning problem of medical statistics so admirably expressed by Dr Prescott.[13] *The Lancet* is to be congratulated on making all this possible.

I. N. MARKS
S. BANK
J. H. LOUW

Groote Schuur Hospital,
Observatory, Cape, South Africa

GYNÆCOMASTIA WITH CIMETIDINE

SIR,—Hall[1] and Sharpe and Hawkins[2] have reported breast pain and gynæcomastia when treating Zollinger-Ellison syndrome and peptic ulcer disease with H_2-receptor antagonists. In two cases thorough endocrine studies were done, including prolactin assay, but no abnormalities were found.[1] We have measured the plasma-prolactin by radioimmunoassay in six patients with duodenal or post partial gastrectomy anastomotic ulcers or Zollinger-Ellison syndrome. Plasma-prolactin was measured before and at the end of 2 months' cimetidine treatment (0·4 g by mouth, four times daily) Patients were not receiving any other drug.



Plasma-prolactin (hPRL) before (a) and after (b) cimetidine.
The sex, age, and diagnosis of the patients were: (1) M, 30, Zollinger-Ellison; (2) F, 58, Zollinger-Ellison; (3) M, 57, post-gastrectomy; (4) M, 52, duodenal; (5) M, 38, duodenal; (6) F, 27, post-gastrectomy.

The results obtained are shown in the figure. Pre-treatment values were normal (5–15 ng/ml in males and 5–20 ng/ml in females). At the end of the treatment the plasma-prolactin had risen by 50–112%. One patient had gynæcomastia and a young woman had galactorrhœa.

These results offer a possible explanation for the side-effects of H_2-receptor antagonists at mammary-gland level. The mechanism responsible for the increase of prolactin is unknown.

G. F. DELLE FAVE
G. TAMBURRANO
LAURA DE MAGISTRIS
CLARA NATOLI
M. LUISA SANTORO
R. CARRATU
A. TORSOLI

Gastroenterology and Endocrinology Units,
2nd Medical Clinic,
University of Rome,
00100 Rome, Italy

1. Hall, W. *New Engl. J. Med.* 1976, **295**, 841.
2. Sharpe, P. C., Hawkins, B. W. *in* Cimetidine: Proceedings of 2nd International Symposium on Histamine H2-receptor Antagonists; p. 358. Amsterdam, 1977.

CONSTITUTIONAL UNCONJUGATED HYPERBILIRUBINÆMIA

SIR,—Dr Bailey and his colleagues (April 30, p. 391) suggest that the hyperbilirubinæmia found in Gilbert's syndrome is not a real disease but rather constitutes the upper end of the normal range. This view implies that all patients with unconjugated hyperbilirubinæmia in the absence of overt bilirubin overproduction belong to a homogeneous group, which is neither our experience nor that of others.[1]

Over the past five years we have investigated 39 patients with chronic unconjugated hyperbilirubinæmia which could not be explained by overt dyserythropoiesis or hæmolysis. 36 of these patients closely resembled each other in having a normal (slightly reduced in 2 cases) plasma disappearance-rate of bromsulphthalein and much reduced hepatic bilirubin/uridine-diphosphate glucuronosyltransferase activity (B.-G.T.A.), a finding reported by others.[2,3] The B.-G.T.A. in these patients was 0·25±0·17 (S.D.) mg bilirubin conjugated/h/g liver, the normal value in our laboratory being 1·33±0·44. However, chronic unconjugated hyperbilirubinæmia was also observed in 3 brothers whose features were different from the other 36. Their plasma disappearance-rates of bromsulphthalein were dramatically reduced (0·04, 0·05, and 0·05) compared with our normal value of 0·14±0·02, while the B.-G.T.A., measured in one brother, was normal (0·874). Such patients resemble those described by Martin et al.,[1] who also had unconjugated hyperbilirubinæmia and very low disappearance-rates of bromsulphthalein; B.-G.T.A. was not measured.

These findings demonstrate that there are at least two types of constitutional unconjugated hyperbilirubinæmia—one associated with a reduced B.-G.T.A., while the other, a rare condition, seems to be primarily related to a defect in hepatic uptake. People with constitutional unconjugated hyperbilirubinæmia therefore form a heterogeneous population, a factor not considered by Dr Bailey and his colleagues.

J. -M. METREAU
D. DHUMEAUX
C. GISSELBRECHT
A. -M. PREAUX
P. BERTHELOT

Unité INSERM U-99 and
Service d'Hépatogastroentérologie,
Hôpital Henri Mondor,
94010 Creteil, France

SCHIZOPHRENIA AS A PROSTAGLANDIN-DEFICIENCY DISEASE

SIR,—While Dr Horrobin (April 30, p. 936) refers to some interesting observations on the resistance of schizophrenics to rheumatoid arthritis and other inflammations as well as a possible higher tolerance of pain, the hypothesis that schizophrenia is a prostaglandin-deficiency disease leaps too far. Although prolactin release may be a prostaglandin stimulant not all antischizophrenic drugs lead to increased prolactin secretion, as he claims. Clozapine is a prime example of a non-prolactin-releasing, antischizophrenic agent. Moreover, other prolactin releasers, such as methyldopa and tricyclic antidepressants, are ineffective in schizophrenia. Recent findings from the University of Louisville[4] show that dialysis may help schizophrenics. This would imply that the disease may be that of an excess of an abnormal constituent, rather than a deficit. The absence of rheumatoid arthritis in schizophrenics could be explained by a protective effect of the excess substance against possible infective agents (considered by many as the probable cause of rheumatoid arthritis) or by a general anti-inflammatory action. Finally, normal doses of analgesic anti-inflammatories suppress protaglandin synthetase yet do

1. Martin, J.-F., Vierling, J. M., Wolkoff, A. W., Scharschmidt, B. F., Vergalla, J., Waggoner, J. C., Berk, P. D. *Gastroenterology*, 1976, **70**, 385.
2. Black, M., Billing, B. H. *New Engl. J. Med.* 1969, **280**, 1266.
3. Felsher, B. F., Craig, J. R., Carpio, N. M. *J. Lab. clin. Med.* 1973, **81**, 829.
4. Wagemaker, H. Presented to the annual meeting of American Society for Clinical Pharmacology and Therapeutics, held in Dallas, Texas, in 1977.