Correspondence

Correspondents are asked to be brief.

Specialty of Haematology

SIR,—Your leading article on this subject (27 June, p. 743) contains certain statements, particularly regarding the attitude of the Royal College of Pathologists, upon which I would like to comment. In the first place you give an impression that there is virtual unanimity among haematologists as to the training and examination structure that they consider ideal for their specialty. This is far from being the position, and it is because this College has been hearing strongly conflicting opinions on these matters that its response has been, as you say, "muted." In short, we have thought it wise to weigh the case for change carefully and to consider all the suggested directions of change in some detail before altering a system that has undoubtedly within a few years markedly raised the standards of haematological practice in Great Britain.

This College has, since its founding in 1962, designed its training recommendations and its examinations with the object of ensuring that a successful candidate is competent to take charge of a laboratory concerned with his specialty and to advise on the clinical implications of his work. The appointments recognized in haematology departments have included duties in anaemia clinics and the examinations include the testing of a candidate's knowledge of the clinical aspects of his specialty.

To state, as you do, that "The Royal College of Pathologists . . . does not distinguish between the fields of activity of its members" is so far from the truth that I cannot conceive how you came to print it. From the start the College has insisted that the branches of pathology are separate specialties and that it is unreasonable to expect a specialist in one to deputize in another or to make appointments requiring practice at consultant level in more than one laboratory specialty. The final examinations in the specialties are entirely different and each has been progressively modified over the seven years since they commenced. They have, however, retained the common objective of ensuring satisfactory completion of training in the special branch, including competence to take charge of a laboratory. Once we are confident that the correct formula has been found for modifying any of these schemes we shall not hesitate to make changes.

Your statement that most of the members of the Royal College of Pathologists are histopathologists, which must have been a guess, is also inaccurate: it is possible to determine the proportion with accuracy only for those who have entered the College by examination and of these 43% are histopathologists, 24% haematologists, 20% microbiologists, and 13% chemical pathologists.—I am, etc.,

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Barbiturate-induced Injection Lesions

SIR,—The contents of proprietary barbiturate capsules including Tuinal[R] and Nembutal[R] are not entirely water-soluble, and unless particles are removed prior to injection of solutions prepared from such material, as for instance by insertion of a cotton plug in the syringe, then mechanical irritation may ensue.

However, a far more significant factor in relation to the necrotic ulcerating lesions in those who inject barbiturates intravenously as described by Dr. Dorothy I. Vollum (13 June, p. 647) would appear to be the alkalinity of such solutions. The *p*H values of aqueous solutions of sodium salts of barbituric acid derivatives are high: a 10% (w/v) solution of sodium amylobarbitone in water has a *p*H value of about 11. The corrosive effect on the gastric mucosa of the soluble barbiturates is familiar to all pathologists in cases of fatal overdosage, and further, though alkaline solutions of thiopentone sodium, for example, may be injected intravenously, it is known that extravasation is liable to cause tissue necrosis. Another contributing factor, especially if injections are made subcutaneously rather than intravenously, may be the hypertonicity or hypotonicity of the solution. A 4·07% (w/v) aqueous solution of amylobarbitone sodium is isotonic.

We suggest that the alkalinity of the solution is the prime cause of the necrotic lesions seen in those who self-administer by injection barbiturates intended for oral use.—We are, etc.,

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Insulin Mixtures and Hypoglycaemia

SIR,—Recently, a diabetic patient under my care was involved in a serious car accident as a result of a hypoglycaemic episode when he was driving to work.

The patient was usually well controlled on 30 units of protamine zinc insulin and 16 units of soluble insulin, and the only relevant fact which emerged on close questioning was that the patient had been mixing the two insulin preparations in one syringe prior to injection. When asked where he had obtained such instructions, he referred to the drug manufacturers' leaflet. Discussing mixtures of long-acting and soluble insulin, these instructions were as follows: "When a mixture of soluble insulin with these insulins is used, inject air into the bottle of depot insulin but without inverting it or withdrawing the dose. Next, inject air into the bottle of soluble insulin and withdraw the dose in the usual way; then reinsert the needle into the bottle of Protamine Zinc insulin or Isophane insulin and

withdraw the dose into the same syringe."

Three out of four manufacturers of insulin give almost identical instructions. Only A.B. Insulin Ltd. state: "Never change the type of insulin or the dose, or mix one type of insulin with another, except on the instructions of your doctor. . . ." One well-known textbook[1] dealing with the subject of mixtures of soluble insulin and protamine zinc insulin states: "The two insulins can be given either as separate injections or mixed in the proper proportion immediately prior to injection." The Action and Uses Section *B.P/B.P.C.*[2] after discussing the use of protamine zinc insulin goes on to state ". . . a dose of unmodified insulin is often given at the same time to tide over the period until the protamine zinc insulin is absorbed: the two insulins may be mixed in the syringe immediately before the injection is given."

Malins, writing in *Prescribers' Journal*,[3] discusses protamine zinc insulin and states: "P.Z.I. is still widely used though it contains an excess of protamine that will convert a proportion of any soluble insulin which may be added to it into the long acting form. Nevertheless, P.Z.I./S.I. mixtures have been surprisingly successful. . . ." On the other hand, a standard textbook of therapeutics[4] discussing the same subject states: ". . . . some insulin preparations . . . cannot be mixed with one another in the same syringe as this would alter their normal times of action—for example, soluble insulin and protamine zinc insulin."

It is apparent that there is a difference of opinion regarding the mixing of soluble and protamine zinc insulin. In my view such mixtures introduce a degree of unpredictability in the time of action by reason of the variable combination of soluble insulin with the excess protamine present in protamine zinc insulin.

Whatever our views, three out of four major manufacturers of insulin make no allowance for such differing opinions in the instructions which they enclose with their insulin preparations. The purpose of this communication is to bring this to the notice of members of the profession who may be unaware at present of the manufacturers' directions, and to promote a more uniform point of view so that the risk of patients receiving conflicting advice may be minimized.—I am, etc.,

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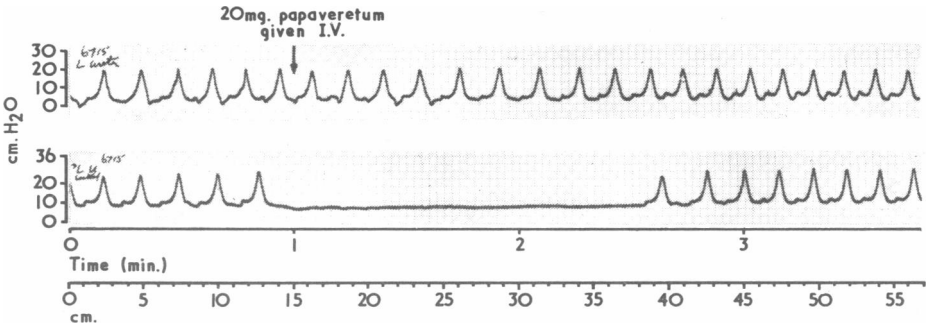
REFERENCES

1 Sayers, G., and Travis, R. H., in *The Pharmacological Basis of Therapeutics*, ed. L. S. Goodman and A. Gilman, 3rd edn.; p. 1592. New York, Macmillan, 1965.
2 *British Pharmaceutical Codex 1968*, p. 397. London, Pharmaceutical Press.
3 Malins, J. M., *Prescribers' Journal*, 1970, **10**, 25.
4 Duncan, L. J. P., in *Textbook of Medical Treatment*, ed. D. Dunlop, S. Alstead, and A. G. Macgregor, 11th edn., p. 347. Edinburgh, Livingstone, 1968.

Morphine a Spasmolytic?

SIR,—In your interesting and valuable article on "Narcotic Analgesics—II. Adverse Effects" (6 June, p. 587) it is mentioned that morphine and most of the other narcotics cause spasm of the biliary and renal tracts but in a sufficient dose they will relieve colic. This is no doubt correct in most instances, but morphine derivatives can relax the plain muscle of the ureter in some patients.



Woman (aged 31). Right-sided pyelitis. Consecutive tracings from normal left ureter showing effect after injection of 20 mg. papaveretum intravenously. The peristaltic wave has been made to disappear for almost two minutes.

In our study of ureteral peristalsis in human patients recording the activity of the ureter by linking a strain gauge and recording apparatus to a system of injection of radio-opaque solution in the course of retrograde pyelography[1] we have observed the action of various drugs on the ureter.[2] Antispasmodic drugs such as atropine, buscopan, and pethidine slow down the rate and reduce the height of the peristaltic wave, and abolish it sometimes. Papaveretum does the same in some patients, as the enclosed tracing demonstrates, relaxation, not spasm, being produced.

It is possible that this particular action may be one of the ways in which morphine and its derivatives gives relief in renal colic cases.—We are, etc.,

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REFERENCES

1 Ross, J. A., Edmond, P., Coull, J., and Griffiths, J., 1967, *Journal of Urology*, **97**, 449.
2 Ross, J. A., Edmond, P., and Griffiths, J. M. T., 1967, *British Journal of Urology*, **39**, 26.

Typing the Gonococcus

SIR,—During a recent investigation into certain properties of *N. gonorrhoeae* it was found possible to classify the organism into different serological groups, using a similar technique to that of Lancefield[1] for the classification of haemolytic streptococci. Antisera were produced by the intravenous inoculation into rabbits and cockerels of suspensions of gonococci. The crude serum invariably had to be absorbed to avoid cross-precipitation with other groups.

Of the 181 strains of *N. gonorrhoeae* examined (with five different antisera) 143 strains could be classifed into one or other of five serological groups. Thirty-eight gave no reaction to any of these five antisera (N.G.=non-groupable), but other groups than the five could no doubt be developed if further antisera were made. Forty-three strains (M.G.=multi-group) gave positive precipitin tests with two or more of the absorbed sera, suggesting that the patient probably had a "mixed infection."

The strains examined came from varying places: Southampton, Birmingham, Portsmouth, Aldershot, Liverpool, London, and one unknown source. They were classified as follows:

Group A	(8)	=	4·4%
Group C	(45)	=	24·86%
Group D	(7)	=	3·8%
Group E	(30)	=	16·57%
Group F	(10)	=	5·52%
Group M.G.	(43)	=	23·75%
Group N.G.	(38)	=	20·99%

It was found that repeated subculture caused the gonococcus rapidly to lose its specificity so that it was necessary repeatedly to take a "group" strain from recently isolated and tested organisms to keep as the stock strain for control tests and for antiserum production. Lypholized strains always gave clear-cut results when reconstituted.

Examination by this method of all strains of *N. gonorrhoeae* isolated throughout the country would add much to the knowledge of the epidemiology of gonococcal infections, especially if methods of "typing" within the groups could be developed as was done in the case of the haemolytic streptococcus.

The technique of the test is very simple and is used in nearly all laboratories in the country for the grouping of haemolytic streptococci.

The work described above was done during the holding of the Insole Research Award, B.M.A., 1967.

—I am, etc.,

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REFERENCE

1 Lancefield, R. C., *Journal of Experimental Medicine*, 1933, **57**, 571.

Migrating Intravenous Catheter

SIR,—In 1964 the secretaries of the medical protection organizations issued a communiqué[1] drawing attention to the dangers of disruption of plastic intravenous catheters, particularly those which are inserted through the needle; this was occasioned by previous reports of this mishap. We think it appropriate to re-emphasize this danger by reporting the following case.

A 23-year-old pregnant woman was admitted to a London hospital suffering