accurate list of these questions and I cannot agree with Professor Kekwick that 90% have been clinical. Indeed, I would put the true figure as at most 30%. But I would not be in the least surprised to know that the professor has some peculiarly personal definition of the word "clinical." Would he regard the following sample question, which was one recently asked, as clinical or as a sadistic joke at the candidate's expense, and not to be taken seriously?

Which of the following is correct?

Kala-azar is black man's disease

Kwashiorkor is red dog disease

Polycythaemia rubra vera is homme rouge.

But let the R.C.P. allow your readers to judge for themselves by publishing the first and second group of multiple-choice questions. Why the secrecy?

Professor Kekwick informs us that "the members of the examiners' panel themselves have sat the multiple-choice questions." Sitting an examination means nothing. What of the results? Are these also secret? There is a widespread rumour that some of the examiners did very badly. Is this true? This may not be anything of which to be ashamed, if the questions were indeed stupid. On the other hand, how many of the examiners themselves had to take the M.R.C.P. examination more than three times before achieving success?

My question as to why the pass list has altered from less than 5% to 20% remains unanswered. Is this another secret?

How many Afro-Asians have taken the examination during the last 10 years? How many of them (excluding those qualified in England) have been successful? Is this also a secret?

Why should the M.R.C.P. of Australia exempt candidates from two parts of the new examination, but the M.R.C.P.s of Edinburgh or Glasgow not exempt even from one part? Are the reasons for this also a secret?

Why under the new regulations are only two specialties recognized—namely, psychiatry and paediatrics?

Why . . . why . . . etc., etc. I could fill pages of your journal with such questions about which the R.C.P. remains silent and secretive.—I am, etc.,

London W.1.

M. H. PAPPWORTH.

Sulphonylurea Drugs in Pregnancy

SIR,—Recorded experience with sulphonylurea drugs in diabetic pregnancy has so far been scanty and confusing. Jackson and his colleagues¹ reported a foetal loss rate of 50% in a group of 40 patients treated with sulphonylurea compared with 20% in a control group treated with insulin or diet only. He attributed the excess mortality to the use of chlorpropamide in a dose of 500 mg. daily. Nearly half the patients were more than 35 years old, and all but three were known diabetics before becoming pregnant. Dolger and his co-workers² treated 52 patients with abnormal glucose-tolerance tests in pregnancy with a foetal loss of 7.7%. The average age was said to be less than in Jackson's series.

The reason for anxiety about the use of sulphonylurea drugs in pregnancy is the possibility of damage to the foetus either by a teratogenic effect in the early weeks or by a more obscure process in the later stages.

Theoretically these drugs can cross the placenta and might have a direct effect on the foetal islets of Langerhans. The Rare Diseases Subcommittee of the Medical and Scientific Section of the British Diabetic Association has in the last year collected reports from clinics in Britain of 41 diabetic women treated with sulphonylurea drugs in pregnancy (see Table). We have divided them into two groups:

Group A.—Twenty-three women treated with drugs throughout the first and second trimester. Twenty-two were already being treated for diabetes at the time of conception. One was diagnosed in the first month of pregnancy (15 took chlorpropamide and 8 tolbutamide).

Group B.—Eighteen women treated with drugs in the last trimester only (11 took chlorpropamide, 5 acetohexamide, and 2 tolbutamide).

Results	No.	Mean Age (Years)	Diagnosis		Result			Foetal Deformity
			Clinical	Latent	Live Birth	Still-birth	Neo. Death	
Group A	23	31	22	1	22	1	—	1 accessory auricle
Group B	18	32	5	13	12	5	1	None

The daily dosage in the cases of foetal death was as follows:

Group A: Stillbirth, chlorpropamide 375 mg.

Group B: Stillbirth, chlorpropamide 500 mg.; stillbirth, chlorpropamide 250 mg.; stillbirth, tolbutamide 1.5 g.; stillbirth, tolbutamide 1 g.; stillbirth, acetohexamide 500 mg.; neonatal death, chlorpropamide 100 mg.

Clearly the number of cases is too small to permit conclusions from the data presented here. The following tentative comments are offered:

(1) There is no evidence of a teratogenic effect of sulphonylurea drugs in the dosage usually employed in the human subject.

(2) There is as yet insufficient evidence to show whether these drugs have a harmful effect in the later stages of pregnancy.

The apparent difference in the outcome of pregnancies in *Group A* from those in *Group B* cannot be explained because the numbers are small. It does perhaps accord with the observations of Pedersen and Brandstrup³ that women reporting early in pregnancy have a lower foetal loss rate than those who come late, for all but 3 of the women in *Group B* had no treatment in the first six months of their pregnancy.

We wish to thank all those members of the Medical and Scientific Section of the British Diabetic Association who submitted case reports.

—We are, etc.,

J. M. MALINS,

Chairman.

A. M. COOKE.

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Neonatal Thrombocytopenia and Thiazide Drugs

SIR,—The hazard to the foetus of thiazide administration to the pregnant mother is now under discussion again.¹⁻³ In view of the widespread use of thiazides in the treatment of toxæmia of pregnancy it is appropriate to be concerned about this problem.

As a possible mechanism to explain drug-induced neonatal thrombocytopenia, you suggest in your leading article (30 May, p. 1395) that perhaps "there is some concentration of the drug on the foetal side of the placenta," and that "we need to know more about the findings in the blood of infants of mothers treated with these oral diuretics. . . ." Your suggestion has a basis in more than supposition for the transplacental transfer of chlorothiazide was postulated by your expert consultant last year,⁴ and has also been demonstrated by J. Garnet⁵ in a study carried out on 19 patients. His data indicated that chlorothiazide is transferred readily across the placental membrane and is found to attain levels in foetal blood plasma comparable to those in maternal blood plasma. J. Harley and co-workers comment on this aspect of the problem in their letter on haematological abnormalities in two newborn infants entitled "Thiazide-induced Neonatal haemolysis?" which appeared in your journal several months ago (14 March, p. 696).—I am, etc.,

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- 3 *Canad. med. Ass. J.*, 1964, **90**, 1278.
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Treatment of Typhoid Carriers

SIR,—Dr. A. B. Christie (20 June, p. 1609), in his article "Treatment of Typhoid Carriers with Ampicillin," states that massive penicillin therapy with or without sulphonamides is ineffective and he also questions the significance of the Vi-agglutination test. There was to my knowledge one female patient in a mental hospital who, 17 years ago, was cured by massive penicillin and sulphathiazole treatment and is of interest because I happened to follow up her serum Vi-agglutinin titre for several years after her cure. The patient was No. 4 in the list of 17 typhoid carriers treated by Fry *et al.*¹ She had been a heavy faecal carrier of *Salmonella typhi* Vi-phage type E1 for at least six years and had a cholecystectomy two years before her treatment. At the time the article was written she had ceased carrying for 36 weeks, but her Vi-agglutinins had remained unchanged over this period. Specimens of faeces were examined at weekly intervals for one and three-quarter years after her cure. She was then transferred from a single-bedded ward to a general ward and specimens of faeces were examined at intervals after transfer, but none revealed *Salm. typhi*. There were no cases of typhoid fever in the hospital following her treatment. She was an inmate of the hospital for 39 years, and was cured of the carrier state 13 years before her death at the age of 74 years.

Serum was collected at approximately six-monthly intervals, and aliquots of each speci-