ml. Protein electrophoresis showed an increase of alpha-2 globulin with a decrease of gammaglobulin. Urine: massive proteinuria, mostly albumin.

The patient was treated with antibiotics and prednisolone and responded well. He had been admitted to another hospital at the age of 2 years with typical features of nephrotic syndrome, which was confirmed by the appropriate investigations. He had received a course of prednisolone which was finally discontinued one year later. He had been in remission up to his present episode. Detailed inquiry showed that before his first admission to hospital he had been immunized against measles. Five days afterwards he became feverish and developed conjunctivitis, which did not respond to topical antibiotics, and three days later his mother noted generalized oedema and swelling of his eyes. During the first year of life he had had recurrent attacks of wheezy bronchitis for which he required bronchodilators. There was family history of bronchial asthma but not of other allergies.

These two children are atopic subjects who should not have had measles vaccination. Nevertheless, it is surprising that the nephrotic syndrome has not been reported previously. Possibly accurate medical histories were not obtained. If these observations can be substantiated by others, and since the nephrotic syndrome is not known to occur after natural measles, it would suggest that other factors in the vaccine are involved which might offer a useful line of research into the elucidation of the basic nature of this disorder.

Since these observations were made a third case similar to the above has been seen.—I am, etc.,

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1 Department of Health and Social Security. *Circular Letter* CM07/70 July, London, D.H.S.S., 1970.
2 *British Medical Journal*, 1968, **1**, 395.

Rubella Vaccination and Termination of Pregnancy

SIR,—There have been few reports from Britain of inadvertant rubella vaccination in pregnancy. For this reason the report of Drs. Hélène J. Mair and A. R. Buchan (4 November, p. 271) is important in that it draws attention to the problem and stresses that rubella vaccine should be given only to women who are seronegative, who are not pregnant, and who have been warned of the possible risk involved if they should become pregnant in the next two months. In my experience, inadvertent rubella vaccination during pregnancy is seen more commonly than is rubella in pregnancy. If this is generally so, then publishing national figures of abortions performed because of inadvertant rubella vaccination in pregnancy, as suggested by Drs. Mair and Buchan, would help to draw attention to the extent of this preventable iatrogenic disease.

The risks of rubella vaccination in pregnancy cannot be known until all cases of women being inadvertently vaccinated are carefully documented, the products of conception examined virologically, and any children born followed up for at least five to seven years for any signs of the expanded congenital rubella syndrome. The following figures from the world literature until October 1972 may help family practitioners and gynaecologists to advise patients who are vaccinated just before or during early pregnancy.

No cases of embryopathy due to rubella vaccine have been reported. Only three cases of fetal infection with rubella virus have been reported—attenuated rubella virus was isolated from the kidney (and from only the kidney) of one fetus,[1] from the femoral bone marrow (and from only the femoral bone marrow) of another,[2] and from the eye of another.[3]

In 60 women who were known to be seronegative before inadvertent vaccination just before or during pregnancy, or before vaccination in women who were to have legal abortions, [1 2 4-10] rubella virus was obtained from only two fetuses[1 2] and from the placenta or decidua of only seven.[1 8]

Of the 37 women known to have been seropositive before vaccination,[1 9] no virus was obtained from the products of conception of the 35 who had spontaneous or induced abortions, and the two babies born were described as being apparently normal.[9]

Of the 70 women whose immune status was not known before vaccination,[11 12] the virus was obtained from the placenta or decidua from two women. Histological lesions similar to those found in rubella were noted in the placentas from these two women and from one other patient.[11] It was reported that nine women were still pregnant and that the 10 babies already delivered were apparently normal.[12]

The United States Center for Disease Control[3] summarized the reports it had received until October 1971 of 193 women vaccinated in pregnancy. Because some of the cases listed above might also have been included with these, the figures are given separately. There were 171 women whose immune status was not known before vaccination. From the products of conception of the 97 of these who had spontaneous or induced abortions no virus was obtained. Of the remaining 74, 56 had delivered apparently normal live babies and 18 were still pregnant. Of the 22 women known to be seronegative before vaccination, rubella vaccine-like virus was found in the decidua or placentas of three, and in one of these cases the virus was isolated from the eye of the fetus.[3] Eight had delivered apparently normal babies and one was still pregnant.

None of the babies born to mothers who were vaccinated during pregnancy showed evidence of the congenital rubella syndrome; reports of the births of 64 such babies have been made by the United States Center for Disease Control,[3] of 38 by Gold,[13] of 10 by Cooper,[12] and of another 10 by others.[9 11 14 15]—I am, etc.,

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1 Vaheri, A., *et al.*, *New England Journal of Medicine*, 1972, **286**, 1071.
2 Ebbin, A. J., *et al.*, *Lancet*, 1972, **2**, 481.
3 Center for Disease Control, *Rubella Surveillance*, United States Department of Health, Education and Welfare, Atlanta, Georgia, October 1971, No. 3, p. 12.
4 Prinzie, A., Huvgelen, C., Gold, J., Farquhar, J., and McKee, J., *American Journal of Diseases of Children*, 1969, **118**, 172.
5 Furukawa, T., *et al.*, *American Journal of Diseases of Children*, 1969, **118**, 262.
6 Katz, S. L., *American Journal of Diseases of Children*, 1969, **118**, 317.
7 Halonen, P., *American Journal of Diseases of Children*, 1969, **118**, 317.
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10 MacDonald, H., Thompson, K. M., and Tobin, J. O'H., *Practitioner*, 1971, **207**, 57.
11 Larson, H. E., Parkman, P. D., Davis, W. J., Hopps, H. E., and Meyer, H. M., *New England Journal of Medicine*, 1971, **284**, 870.
12 Cooper, L. Z., *Canadian Journal of Public Health*, 1971, **62**, (September Monograph Supplement), p. 48.
13 Gold, J., *Canadian Journal of Public Health*, 1971, **62**, (September Monograph Supplement), p. 68.
14 Chin., J., Ebbin, A. J., Wilson, M. G., and Lennette, E. H., *Journal of the American Medical Association*, 1971, **215**, 632.
15 Editorial Comment, *Obstetrical and Gynaecological Survey*, 1971, **26**, 235.

SIR,—I would like to record a further three cases of rubella vaccination during pregnancy in support of the recommendations of Drs. Hélène J. Mair and Alan R. Buchan (4 November, p. 271).

In the first case the nature of the vaccine had been misunderstood and it was administered to a patient known to be eight weeks pregnant because she had been in contact with a case of rubella. As soon as the error was discovered the patient was referred for termination and the conceptus was aspirated at 10 weeks. No virus was isolated from either placental or fetal tissue which was submitted for examination. In the second case the patient became pregnant six weeks after rubella vaccination. Aspiration of the conceptus was performed at eight weeks and again no virus was isolated from the products of conception. The third case was estimated to have conceived 60 days after administration of the rubella vaccine and it was decided to allow the pregnancy to continue. The patient has subsequently given birth to an apparently normal child.

The virological studies were kindly performed by the virus diagnostic laboratory at the Preston Royal Infirmary.—I am, etc.,

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Exposure to Rubella in Pregnancy

SIR,—Sometimes a pregnant woman is exposed to infection from rubella in her own child. Maternal concern is such that blood is often taken within 14 days of the earliest possible date of infection—that is, within too short a time for antibodies to appear as a result of infection from the child.[1] Should antibodies be found it is rightly concluded that there had been no risk from the child, since immunity had already been established. But there are two other possibilities: (1) the mother may have had a subclinical infection and passed on the virus to her child, who then developed the full clinical picture; (2) mother and child may have been infected from the same source. There is all the more reason to think of these possibilities when the child is so young that probably it has met with others only when with its mother.

An 18-month-old girl was seen with what was considered to be typical rubella. Her mother, aged 22, was 18 weeks' pregnant. She gave a precise history of having herself suffered twice from rubella as a child. Notwithstanding, on the second day of the child's rash the doctor took blood from the mother. This was found to have antibodies at the upper limit of the routine test used in the laboratory. The serum was therefore retested, using a higher range of dilutions. The titre which emerged was, in the light of the experience of the laboratory, thought to be suggestive of fairly recent infection. At no time did

the mother have a rash, fever, adenitis, or arthralgia. A second blood sample was tested in parallel with the first after 10 days. The two showed the same somewhat high level of haemagglutination inhibiting antibodies.[2] (There was a two-fold reduction in the titre of the first serum after treatment with 2-mercaptoethanol for the removal of IgM antibodies.[3]) In the absence of any rise in titre a complement fixation test was done. The result was a two-fold rise in titre—not in itself diagnostic, but the actual level of complement fixing antibodies was relatively high (1/64 and 1/128). These results were interpreted to mean that the patient had "recently been infected with the rubella virus." The pregnancy was terminated. Rubella virus was grown from the lung, kidney, and placenta of the products of conception.

When a pregnant woman thought to have been in contact with rubella has no antibodies there is no question of what to do next. When antibodies are found, indicating infection at some time, a problem may arise. This cannot be settled by determining their actual level in a single specimen. There is no absolute figure which is diagnostic of an infection just acquired—not even within a single laboratory using the same method day-by-day, with the utmost care to be consistent. There is variation in the individual immune response to infection and also in the biological materials used in the test for the antibodies which are produced. Therefore the titre of a serum must be considered in the light of the circumstances of the case in order to decide whether the infection may be recent. If so a crisis arises. The case described here shows what may be done to resolve it.—I am, etc.,

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1 Dudgeon, J. A., *British Medical Bulletin*, 1969, 25, 159.
2 Stewart, G. L., *et al.*, *New England Journal of Medicine*, 1967, **276**, 554.
3 Banatvala, J. E., Best, J. M., Kennedy, E. A., Smith, E. E., and Spence, M. E., *British Medical Journal*, 1967, **3**, 285.

Duodenogastric Reflux and Pyloric Surgery

SIR,—One of the unfortunate aspects of this debate is that pyloric reflux and gastric retention have been proposed as opposing theories in the aetiology of gastric ulcer, whereas they are probably both features of the same underlying pathology. As Mr. H. W. Burge points out (11 November, p. 360), duodenal and pyloric channel disease could give rise to both and, in the presence of a normal pylorus, the antroduodenal motility patterns that are associated with reflux[1] would also tend to delay gastric emptying. The length of time that refluxed duodenal juice remains in the stomach may determine the degree of mucosal damage. It must also be remembered that there are three types of gastric ulcer, possibly with different causes.[2]

If the gastric ulcer is clearly secondary to duodenal or pyloric disease (Type II) and the acid secretion is moderate or high, then vagotomy is theoretically a reasonable operation to heal the duodenal ulcer. But ulcers cause scarring when they heal and a scarred duodenum and pylorus may perpetuate a delay in gastric emptying and a pyloroplasty may be required in addition.

With the primary lesser curve ulcer (type I), for those who suggest that the main problem is increased antral gastrin release following gastric stasis the two logical alternatives are a Billroth I antrectomy or an adequate simple drainage operation, but the latter has not proved effective. We would suggest that a proximal gastric vagotomy without drainage does not follow logically from the hypothesis of gastric stasis in patients without associated duodenal or pyloric disease. For those who think that reflux is the primary problem the logical operation is a Roux-en-Y reconstruction (with vagotomy to protect the jejunum). The alternatives are: (*a*) an operation that allows little reflux, and this is probably provided by a Billroth I antrectomy with a small stoma; or (*b*) an operation that allows rapid emptying once reflux has occurred, which may be provided by a wide pyloroplasty, but this also gives rise to increased reflux.

If we look at the operations themselves, we find that the great success of the Billroth I[3] operation would support both hypotheses, perhaps favouring the antral gastrin release theory in particular. The moderate success of vagotomy and pyloroplasty[3] also adds some support to both hypotheses, perhaps by overcoming stasis and allowing quick drainage of refluxed duodenal juice, but it is not certain how the vagotomy helps if the night and stimulated gastric acid secretions are already very low. Proximal gastric vagotomy without drainage is logical only if it is thought that a small duodenal or pyloric lesion will heal without scarring and pyloric function and gastric emptying will return to normal.

It is too early in our understanding to be over-dogmatic about one or other aetiological theory or method of treatment, but we should try to make our surgical practice consistent with our theories of the pathophysiology of gastric ulcer and then continually adjust our hypotheses on the basis of a careful analysis of the results of treatment.—We are, etc.,

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1 Johnson, A. G., *British Journal of Surgery*, 1971, **58**, 864.
2 Johnson, H. D., *Annals of Surgery*, 1965, **162**, 996.
3 Duthie, H. L., *Gut*, 1970, **11**, 540.

Hypotension and Methylmethacrylate Cement

SIR,—We have read with great interest the various communications on this subject which have appeared during the past 12 months.[1-7] It would seem that there is still continuing concern regarding the use of acrylic cement in the fixation of prostheses in major hip arthroplasty. Having been responsible during the past 10 years for either the personal administration or supervision of anaesthesia for more than 7,000 hip arthroplasties performed at this centre in which acrylic cement has been used, we feel it may be of some value to present certain of our findings based on this experience.

(1) A fall in blood pressure does not invariably follow the introduction of acrylic cement into either the newly reamed acetabulum or femoral shaft, although it is a common occurrence (80% of cases approximately).

(2) When a fall in blood pressure occurs following insertion of cement into the reamed acetabulum it is small and transient, rarely exceeding 15 mm Hg.

(3) Following insertion of cement into the reamed femoral shaft the fall in blood pressure is usually greater, but rarely exceeds 30 mm Hg. The time taken for a maximum fall to occur is usually 30-60 seconds and there then follows a rapid return to normal, which seldom takes more than a further 90 seconds. We have not noticed the late rise in pressure recorded by Cadle *et al.*[5]

(4) In no instance at this centre has cardiac arrest occurred following the use of acrylic cement, nor have falls in blood pressure given regular cause for concern. Neither are we aware of any patient who has sustained untoward sequelae as a result of the use of the cement. Many of our patients are elderly and frail, and hypertension and coronary artery disease are only too common. Such patients, we agree, compensate poorly following sudden and severe hypotensive episodes, but in our experience the use of acrylic cement does not produce the changes in pulse rate and hypotension which were shown to follow the intravenous injection of monomer into dogs by Peebles *et al.*[2] This is probably not surprising, as the absorption of monomer into the circulation from reamed bone must be considerably slower and blood levels thus proportionately lower. Continuous electrocardiographic tracings carried out on a large number of our patients have never shown any change in character following the use of acrylic cement.

(5) There seems to be conclusive evidence[2 4] that hypotension following the use of acrylic cement is in fact due to the absorption of free monomer into the circulation, and it is interesting to note in this connexion that in our experience no fall in blood pressure follows the use of cement in a knee arthroplasty performed under a tourniquet, a fact already noted by Cole *et al.*[7] From our observations we are convinced that a careful surgical appraisal of the degree of plasticity of the cement prior to its insertion, preceded by a careful technique of preparation, are the important factors which really reduce subsequent hypotension to a minimum. Any departure from this established technique[6] which entails insertion of cement in a more fluid state, particularly into the femoral shaft, will undoubtedly cause a greater fall in blood pressure.

(6) It is not our experience that hypotension following the use of acrylic cement is in any way modified by the choice of a particular type of anaesthetic technique. Over the past 10 years anaesthesia for hip arthroplasty here has embraced all types and combinations of anaesthetic agent, including neuroleptanalgesia, extradural analgesia, and induced hypotensive techniques. Halothane is currently used in combination with other agents in approximately 70% of cases. Nor does the type of operation carried out appear to be significant. A patient undergoing a single uncomplicated hip arthroplasty does not differ in his response to cement from the patient undergoing a bilateral arthroplasty taking up to 3½ hours with a proportionately higher blood loss. Technically difficult conversion arthroplasties, in which there may be extensive reaming of the femoral shaft and relatively higher blood loss, have shown surprisingly little difference in response to cement, though theoretically a greater fall in pressure should be expected in them.

Although we would agree that there is no place for complacency[4] we have not