of somewhat bizarre fibroadenomatous nodules in which it was difficult to differentiate the epithelial from the stromal component. There was some cell atypia and mitotic activity, but in both animals the nodules were well-circumscribed and showed no invasive tendencies. They thus appeared to represent early stages of the benign complex tumour of bitches as described by Conchin. A further observation was the occurrence of active epitheliosis with occasional mictotic figures in some of the ducts and acini in one of the animals, though there was no malignant change.

The appearance of fibroadenomatous nodules at a relatively early age in animals exposed to high dose levels of the natural hormone must, we believe, now give one serious cause to doubt the relevance to the human female of the development of similar nodules in animals given high doses of the derivatives of 17α-hydroxyprogesterone. This view is supported, moreover, by the lack of any real correspondence between the historical appearance of these nodules and mammary carcinoma in the human.—We are, etc.,

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2 Chin, F., Journal of Comparative Pathology and Therapeutics, 1958, 68, 1.

Genetic Cripples

Sir,—Dr. N. J. Gross (17 April, p. 167) rightly criticizes Dr. G. Discombe's estimates (23 March, p. 723) that raising the net reproductive rate (from, say, zero to unity) of patients with X-linked or autosomal recessive conditions will double the number affected in a generation. The doubling time is, as Dr. Gross indicates, a little under four generations for X-linked conditions and it is much more for autosomal conditions for most recessive conditions. Only autosomal dominants will double in one generation.

On the other hand, it is Dr. Discombe who is correct in sensing that the successful introduction of contraception due to mutant genes of large effect poses a real dilemma. The birth frequency of such conditions is in the long run determined by the balance between the loss of mutant genes, from the lowered reproductive rate of the patients, and the gain of mutant genes, from fresh mutation. If improved treatments raise patients' reproductive fitness, say, tenfold, and they choose to make full use of this, the birth frequency of the condition will climb. If things being equal, also rise tenfold. Then loss and gain are once again balanced. Whether the rate of increase be fast or slow, this constitutes a real problem in community health and Dr. Gross's personal view that we can do nothing about it is erroneous. Admittedly we cannot, in the foreseeable future, reduce mutation rates. But no increase whatever in birth frequency of these conditions will occur provided that patients do not make use of their increased fitness to have children. Further, in the case of X-linked and autosomal recessive conditions we may hope to do better still and in time to reduce the birth frequency well below the level maintained by the natural balance.

No authoritative dictum that haemophiliacs should not have children is required. Rather (as Dr. R. Biggs writes—10 April, p. 106) we should fully counsel patients and their relatives on the genetic risks to children and grandchildren and rely on their own good sense to plan their families accordingly. They must, of course, also (as she indicates) be given all necessary help to make their plans effective, including options of abortion and sterilization where appropriate. In one recent follow-up of patients given genetic counselling it was found that no couple planned further children after they had been told that there was a high risk of having a child with haemophilia. On the other hand, some parents were prepared to take the risk of a condition from which the child would certainly die in infancy.

Just at present one would hope that few patients with severe X-linked conditions, including haemophilia, would plan children; but ethically the decision is and should remain theirs to make. However, it is to be expected that, with the help of fluorescent staining, techniques used for Y- and X-bearing sperm will soon be developed. Well-treated haemophiliacs may then reasonably have as many sons as they wish, since these will be unaffected and have unaffected descendents. It would be much less reasonable for haemophiliacs to choose to have daughters since these must carry the gene. If they choose only sons there would be no rise in the birth frequency of haemophilia. Looking further ahead, the discovery in a simple means of detecting carrier girls will provide the opportunity of reducing the birth frequency well below the natural balance at zero reproductive fitness. The natural balance is at a birth frequency equal to three times the mutation rate. Two-thirds are born to carrier mothers, many of whom, if they knew the risk, would plan no children. Further, the discovery of ways of making early prenatal diagnosis of affected male and perhaps of carrier female fetuses, combined with the offer of abortion, would enable such women to have only unaffected sons and only daughters who were not carriers. Only the third of cases due to fresh mutations will then be short of the formidable undertaking of screening all pregnancies. The same techniques of carrier detection and prenatal diagnosis offer the prospect of the virtual elimination of autosomal recessive conditions, since in only a tiny fraction of these is a fresh mutation involved. Only for severe dominant conditions is there little prospect of reducing the birth frequency below the naturally balanced level.—I am, etc.,

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Prostaglandin-induced Labour

Sir,—We read with interest the article by Dr. G. Roberts and Professor A. C. Turnbull (27 March, p. 702), but lest prostaglandin, and uterine hypertonus should somehow become linked in the mind of the reader we would like to emphasize two points in which this report of the use of prostaglandins for the induction of labour differs from previous reports.

Firstly, amniotomy was performed prior to the infusion of the prostaglandin; this was uncommonly done in previous series. In a recent double blind trial of PGE2 and oxytocin in the induction of labour we found it was often necessary to decrease the infusion rate of either drug after spontaneous membrane rupture to avoid uterine over-stimulation. This increased sensitivity of the uterus following membrane rupture may in part explain the hypertonus reported by Dr. Roberts and Professor Turnbull.

Secondly, the doses used at the beginning of the infusion are far higher than usually used. Karim and Filishie have described the sudden increase in tone occurring in the mid-trimester uterus immediately following the infusion of 5 µg prostaglandin/min. We have not commonly seen this, even at that rate of administration, if low doses are used at the beginning of the infusion.

We agree with Dr. Roberts and Professor Turnbull that prostaglandins are powerful oxytocic drugs and endorse the view that great care is needed in their use, lest an undeserved, dangerous name be given to a group of drugs with enormous potential.—We are, etc.,

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Penicillin Allergy

Sir,—In the Therapeutic Conference (3 April, p. 37) Dr. L. Stankler is quoted as saying that a rash "occurs in almost all patients with glandular fever who are given ampicillin." Presumably during the course of glandular fever the mechanisms responsible for the production of an allergic rash are modified in some way. It would be interesting to know if the nature of this modification was known, and also whether it is permanent. Furthermore, should it subsequently be assumed that the patient is allergic to ampicillin (and the other penicillins)?

Ampicillin is not infrequently prescribed for conditions which subsequently turns out to be glandular fever. If the resulting rash is not due to a true permanent allergy, it may be that a very useful range of drugs is being withheld from a group of people in whom they could be used with safety.—I am, etc.,

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Fibrinolytic Systems in Eclampsia

Sir,—The results reported by Dr. J. Bonnar and his colleagues (3 April, p. 12) lend support to the evidence that intravascular coagulation occurs in pre-eclampsia and eclampsia. In their discussion the authors

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