arch, is rarely found. The true congenital flat foot is easily diagnosed very early in life, and here the problem of treatment is entirely different.

It is my experience that unless we distinguish most carefully the deformity which is present and give it its correct descriptive title, we shall be tempted to give treatment which is incorrect, inadequate, and too complex.

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CHRONIC PAROXYSMAL HYPOGLYCÆMIA

SIR,—I should like to thank Mr. Altounyan for reporting (Feb. 11) the interesting history of a case of hypoglycæmia due to an islet-cell tumour of the pancreas, with symptoms for fifteen years prior to operation. It is a pity that a histological report was not available at the time of writing, but presumably the case was one of benign adenoma.

I should, however, like to take issue with the terminology used in the title of the paper.

The term "chronic paroxysmal hypoglycæmia" is nondescript; cases of this sort should be regarded as examples of "hyperinsulinism," as we have recently pointed out.[1] This will avoid unnecessary terms, and enable similar cases to be more easily categorised.

Further, Mr. Altounyan uses the subtitle "Whipple's syndrome." Whipple's disease (intestinal lipodystrophy) was described by *G. H.* Whipple in 1907.[2] Whipple's triad of criteria for the diagnosis of hyperinsulinism were propounded by *A. O.* Whipple in 1935.[3] If an eponym is to be employed, preference could be given to Wilder, who described the first case in 1927 [4]; Harris, who first used the term in 1924 [5]; or Campbell, who did early work on the symptoms of hypoglycæmia in 1922,[6] and was associated with the first successfully operated case in 1929.[7] With such a large field, it is I suggest, preferable to avoid an eponym. Most workers are content with the term hyperinsulinism.

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MYXOMATOSIS

SIR,—Dr. Brailsford (Jan. 14) states: "The Ministry of Agriculture has unsuccessfully used extermination measures for fifty years, at very great cost in value of herds of cattle and flocks of poultry, to get rid of swine-fever, foot-and-mouth disease, and fowl-pest; but it has learnt little or nothing of cure of these conditions though smallpox, cholera, typhoid, plague, and tuberculosis have largely been eradicated without the aid of unprofitable destruction of this type."

The veterinary profession, when dealing with the food-producing animals, has two prime duties: (1) to stamp out any source of infection which may be transmitted to the human population; and (2) to increase the productivity of these animals in order that the nation's larder may be preserved. There are two methods at hand for prevention of disease: (*a*) vaccination; and (*b*) slaughter and the rigid isolation of the affected area. Most bacterial diseases are controlled by vaccination, but most virus diseases have to be controlled by slaughter because of the peculiar characteristics of many viruses existing in several strains and provoking only a short-lived immunity. It is true that we have learned little or nothing of the cure of our virus diseases; but then, has anyone? We cannot cure foot-and-mouth disease, swine-fever, or fowl-pest. I am sure Dr. Brailsford would agree that there is similarly no cure for the common cold, influenza, or poliomyelitis. We can and do protect against swine-fever by vaccination (there is no official slaughter policy against this disease) and we have eliminated foot-and-mouth disease as an enzoötic by slaughter. We have completely eliminated such diseases as glanders, cattle-plague, and rabies by slaughter, and are now eliminating tuberculosis from our cattle population.

It is to be hoped that members of the veterinary profession will never tolerate the slaughter of animals when control by vaccination is an alternative.

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GONADAL DYSGENESIS AND TESTICULAR TUMOURS

SIR,—The recent finding that nuclear sex can be easily determined by the examination of vaginal smears [1–3] has enabled us to investigate systematically cases of primary amenorrhœa. In the course of this work we have come across a patient with a quite unusual clinical picture [4]; to our surprise the cell nuclei in the vaginal smear were chromatin-negative.

A 27-year-old single woman consulted us on account of hirsutism. She had gross features and pronounced virilism. Investigation revealed a calcareous tumour in the minor pelvis, adrenal cortical dysfunction, and increased urinary excretion of 17-ketosteroids. At laparotomy, a solid, fist-size tumour at the site of the left gonad was removed together with the uterus, fallopian tubes, and right gonad. Histopathological examination disclosed that this gonad was rudimentary ("streak ovary"), and the tumour was a dysgerminoma. Postoperatively intensive X-ray treatment of the pelvis was started, and the patient is still well after two years. Ethanol extract of half the tumour mass contained no 17-ketosteroids and but little œstrogenic substance. After irradiation, and possibly as a consequence thereof, the 17-ketosteroid excretion level diminished.

Dysgerminoma is known to be endocrinologically inactive. We therefore assume that in this patient the virilism was caused by dysfunction of the adrenal cortex, similar to that in the adrenogenital syndrome. The fractionated 17-ketosteroid pattern was in full accordance with this assumption.

This case thus presents a striking syndrome, consisting in the combination of: (1) gonadal dysgenesis, proved by the rudimentary gonad and the male nuclear sex; (2) dysgerminoma; and (3) adrenal dysfunction.

The evaluation of recent developments in embryological endocrinology, and study of other cases recently reported, soon convinced us that this peculiar syndrome was not to be regarded as a purely fortuitous coincidence. Patients with so-called "ovarian" agenesis have been shown to be mostly male. It is assumed that in these patients the male gonad, its anlage, or an essential component, must have been destroyed by some obscure early intra-uterine lesion, resulting in completely female sexual development. Although dysgerminoma occurs mostly in normal women, attention has since long been focused on its association with gonadal anomaly and hypoplasia. Novak [5] points out that "dysgerminoma is the most common tumour of pseudohermaphrodites, as it is of males with cryptorchidism." Cryptorchidism also represents a distinct gonadal aberration, occurring in males. Concerning the accompanying adrenal dysfunction Novak [6] and Ber [7] have described cases with hirsutism and virilism, entirely comparable to ours, and dysgerminoma itself is generally believed not to be the source of androgens. It is tempting to assume that the early intra-uterine injury may damage, not only the sole gonadal anlage, but more or less the entire urogenital ridge. This could explain the most varied combined

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morphological or functional aberrations in structures derived from this source : the gonad, the adrenal cortex, and the kidney. Of course, this hypothetical unitarian concept, though supported by several facts, must await further investigation and confirmation.

In 1952 Huddleston Slater [8] described an entirely comparable case in which the patient was later found to have male-type nuclei.[9]

The patient was of normal male habitus, had an empty scrotum, and had been submitted to repeated plastic operations for hypospadias. Laparotomy revealed a normally developed uterus and fallopian tubes and, at the site of the ovaries, bilateral tumours. The right tumour was diagnosed as a differentiated arrhenoblastoma (Pick's adenoma tubulare testiculare ovarii), the left as a dysgerminoma with a separate dermoid cyst. Hormonal findings suggested adrenal insufficiency.

Thus, in this case dysgerminoma was associated with another quite rare tumour, which may arise in ovary or in testis and is thus again associated with undoubted developmental anomaly of the gonads in a male. In males adenoma tubulare has been reported almost exclusively in cases of cryptorchidism or hermaphrodism. In females it is said to exert no virilising effect, but some doubt seems now justified as to whether this tumour is ever found in normal females.

Quite recently Greenblatt [10] described a patient (case 6) with feminine appearance and male skin sex, in whom a testis was removed that contained, amid non-tumorous areas of immature testicular tubules, nodules of adenoma tubulare. The gonadal structure in this case is of special interest, as it seems to represent a transition between the entirely neoplastic right gonad of the foregoing case, and the non-tumorous, immature, œstrogen-producing testes of the so-called "intersex males with purely feminine external genitalia."

These three cases thus present a logical sequence, extending clinically from almost completely male to almost completely female habitus, and histologically from complete aplasia through tumorous aberration to almost normal immature structure. These facts seem to suggest that early intra-uterine injury to the male fœtus may cause either complete destruction with aplasia, or variable damage with eventual tumour formation, or only functional disturbance with no gross morphological aberration of the testis.

Another rare tumour, described as common to ovary and testis, which, in the light of the foregoing, deserves our attention is primary chorionepithelioma of the gonad. The nuclear sex of patients with such a tumour should be carefully studied. This tumour, too, has been reported in conjunction with dysgerminoma, and like dysgerminoma it is often found in young patients.

We can now firmly conclude that some tumours, formerly termed ovarian, are in fact testicular. Some light is thus thrown on the curious identity of dysgerminoma and seminoma. Future studies should be directed to the question whether, taking nuclear sex as a dividing-line, histological difference may be found between tumours that were formerly thought to be identical. On the other hand the evidence points strongly to a close pathogenetic relationship between dysgerminoma and adenoma tubulare.

This seems to represent a new step towards the understanding of various morphological and functional sexual deviations. Male individuals in whom a female or pseudohermaphroditic sexual pattern has developed should be carefully investigated for dysontogenetic tumours.

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"L.E.-CELL" PHENOMENON IN CHRONIC HEPATITIS

SIR,—The article by Dr. Joske and Dr. King [1] in which they report finding L.E. cells in two patients with active chronic hepatitis contains a few points I should like to comment on.

To begin with, it is widely recognised that methods involving the coagulation of blood—such as in the Magath-Winkle [2] procedure adopted in this study—have greatly enhanced the sensitivity of the original L.E. test. Without going here into the reasons for this,[3–7] the question has already arisen whether such techniques should not be used, "because they are so sensitive that they defeat the value of the L.E. cell as an indicator of acute and subacute lupus erythematosus, or whether the method should be welcomed" as a more sensitive but still reliable diagnostic procedure.[8] Also, the need for quantitation of the intensity of the phenomenon has been repeatedly emphasised, and Haserick [9] has remarked that no "aspecific" case has been reported to date, with a strongly positive (++++) plasma-L.E. test. I can add, from my personal experience, that even the degree of homogenisation of the engulfed nuclei has a very great importance, and that greatly depolymerised inclusions after the customary incubation-time, with a marked "jump of coloration" [10] between phagocytosing and phagocytosed nuclear chromatin, clearly indicate a high concentration of the L.E. factor in the blood, and are almost invariably associated with active lupus. L.E.-like cells, "tartoid" cells, and genuine, but generally not plentiful and seldom totally depolymerised, L.E. cells—not to speak of simple nucleophagocytosis—are more frequently met with in non-lupus weakly positive tests, especially by the more sensitive (and often more traumatising) defibrination techniques. In our experience, nucleophagocytosis has been frequent in febrile Hodgkin's disease.

I have accordingly suggested [11] that always at least one defibrinated and one anticoagulant test should be done, the latter preferably both by the auto- and by the iso-techniques (viz., with the patient supplying both the reacting blood or marrow cells and the active plasma or serum factor, or only the latter, the buffy coat being furnished by another, if possible group-compatible, individual, or even by an animal such as the dog or the horse [hetero-test]). In the admittedly rare non-lupus positive tests, good photomicrographs clearly demonstrating at least a couple of typical L.E. cells would also be desirable, since so much information as to the reliability of the report may be gained by simply inspecting these cells. Proof of this may be found in the reported finding of L.E. cells in the ascitic fluids of cirrhotic patients by Leoni,[12] while nothing more than tart cells and the like are depicted in his original article.

Lastly, I agree with Dr. Joske and Dr. King that the L.E. phenomenon may be the end-product of an auto-immune mechanism resulting from true auto-sensitisation, or perhaps simply from antibody-like globulin synthesis with an excessive and disordered immuno-allergic background. In fact, I considered this working hypothesis in 1951 [13] and submitted it more fully in 1952,[14] 1953,[15 16] and 1955.[7 17] This immuno-allergic reaction would seem to develop spontaneously (though it is often precipitated by drugs, stress, or infections), and to be self-perpetuating in genuine

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