to disseminated sclerosis, with the following secondary causes :

	No. of Cases
Disease of the urinary system (with subsequent toxic absorption or uraemia)	12 (21.1%)
Disease of the respiratory system (bronchopneumonia, 15; basal pneumonia, 2; pleurisy, 1; pulmonary embolism, 1; empyema, 2; lung abscess, 1; tuberculosis, 4)	26 (45.5%)
Carcinoma	2 (3.5%)
Perforated peptic ulcer	1 (1.8%)
Death during laminectomy	3 (5.3%)
Cerebral haemorrhage	1 (1.8%)
Overdose of a hypnotic	1 (1.8%)
Aplastic anaemia from arsenical treatment	1 (1.8%)
Disseminated sclerosis involving the medulla	2 (3.5%)
No immediate cause (death ascribed to cachexia and septic absorption from bedsores)	8 (14%)

Here again no conclusions are justifiable beyond the fact that diseases of the urinary and respiratory tracts seem to have accounted for the greater proportion of deaths.

Discussion

An important contribution to the study of the prognosis in disseminated sclerosis has recently been made by Ragnar Müller (1949). He mentions that the literature on this subject "mainly gives casuistic information and reports expressing the respective author's personal opinion, which opinion is not supported by objective facts." Müller conducted a very careful investigation of 810 cases collected from various hospitals in Sweden. He concluded from his results that the prognosis is to a great extent dependent on the type of the initial symptoms, the age at which the patient becomes ill, and also probably, though to a less extent, on sex. He stated :

"When the disease commences with sensory or cranial nervous disorders the prognosis is considerably more favourable than when motility impairments are initial. In the latter case the patients become invalids much earlier. The prognosis is appreciably better when the patients are taken ill at a low than at a high age, in respect to both men and women. This applies even if younger and older persons become ill with symptoms of the same kind. It also seems as if invalidity sets in, on an average, at an earlier age among persons whose illness starts at a high than at a lower age. The prognosis seems to be less good for men than for women. The average lifetime remaining after the incipience of the disease seems to lie between 16 and 34 years.

"From this investigation it cannot be deduced that the changes in the disease picture which are liable to take place in connexion with childbirth are of specially malign character."

Conclusions

It is clear that research regarding the incidence and prognosis of disseminated sclerosis is severely handicapped by inadequacy of the existing case records.

Until accurate notes are available concerning all those suffering from disseminated sclerosis who come under medical supervision (even these being possibly only a small proportion of the total number of patients), no more precise data regarding the onset and prognosis of the disease are likely to become available.

Scrupulous attention to details of early history, as well as the following-up and the long-term observation of patients in all out-patient departments and homes for incurable diseases, is very desirable.

I wish to express my thanks to the National Multiple Sclerosis Society of New York for the very generous grant for this investigation, and to Dr. Macdonald Critchley for his encouragement and helpful criticism. I am also indebted to the authorities in charge of the Putney, Streatham, and Royal Midland Homes for Incurables, and the Richmond Home for Disabled Service Men, who allowed me

to examine and quote their records; to Dr. J. G. Greenfield at the National Hospital; and to Professor P. C. P. Cloake, of Birmingham, who supplied some records of his own cases. I wish also to thank Dr. J. A. Fraser Roberts and Dr. W. J. Martin, of the London School of Hygiene and Tropical Medicine, who so kindly gave their advice and help.

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GYNAECOMASTIA AND TESTICULAR APLASIA

BY

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A case of gynaecomastia with presumed testicular aplasia is described and the reason for the appearance of gynaecomastia in this condition is considered.

Case Report

The patient, a youth aged 17, was referred to me by a colleague, Dr. M. C. Chapman. He complained of pronounced breast development starting at the age of 14. He had not shaved or experienced emissions or erections. He had evinced no interest in members of either sex, but his hobbies had always been those of a boy. He had not had mumps, or disease of or injury to the testicles.

Examination revealed pronounced gynaecomastia (see photograph). The penis was small and the urethra opened at the base of the glans with a patulous orifice. The scrotum was normal and the testicles were normally developed. A sound could be passed down the urethra into the bladder; the prostate could not be felt (Mr. B. H. Page). Pubic hair of feminine distribution was present. Axillary hair was scanty, and the face was covered with a fine down only. His height was 63½ in. (161 cm.), span 66 in. (168 cm.); head to pubis measured 32 in. (81 cm.), and pubis to ground 31½ in. (80 cm.). His manner was retiring and diffident. Urinary gonadotrophins (Dr. A. M. Hain, of Manchester University) amounted to 30 mouse units in 24 hours. Biopsy of the breast by Mr. Page showed hyperplasia of duct elements and fibrous tissue (Dr. J. F. Heggie). Testicular biopsy was refused. A laparotomy, undertaken because the 24-hour excretion of 17-ketosteroids totalled 40 mg., revealed no enlargement or tumour of the adrenals, or tumour of aberrant adrenal tissue anywhere in the abdomen. Subsequent 17-ketosteroid estimations have been within normal limits and the original estimate is believed to have been erroneous. The only adequate treatment of the gynaecomastia is surgical removal, but this his father declined to allow. Treatment with testosterone propionate has not affected the gynaecomastia, but it has led to a quite marked increase in self-confidence and masculine aggressiveness.

Discussion

Gynaecomastia has occurred in workers engaged in the manufacture of stilboestrol and in a number of diseases, the most important of which are tumours of the adrenal cortex, aplasia, destructive lesions and certain tumours of the testicle, and cirrhosis of the liver. Less common causes are pituitary tumours, Albright's disease, and hyperthyroidism; the condition has also followed prostatectomy. In the absence of evidence pointing to any other of these possibilities, the case reported here is presumed to belong to the group of testicular aplasias—probably the commonest cause, anyway. Proof would depend upon testicular biopsy, which has been refused.

Gynaecomastia occurs most characteristically in the type of testicular aplasia described by Klinefelter, Riefenstein, and Albright (1942). Features of this type are aplasia of spermatogenic tissue and Sertoli cells, survival of interstitial tissue with relatively normal androgenic function, a high output of urinary gonadotrophins, and of course gynaecomastia. Heller and Nelson (1945) contrast this with the eunuchoid type in which aplasia of all testicular tissue occurs, including interstitial cells, with greatly diminished androgenic activity; the output of gonadotrophins was increased but gynaecomastia occurred much less commonly. They pointed out the existence of intermediate cases, indicating the essential relationship of the two types.

Castillo, Trabucco, and Balze (1947) reported a third type in which only spermatogenic cells were affected, Sertoli cells and interstitial cells remaining intact. Androgenic activity was relatively normal, gonadotrophin output was normal, and gynaecomastia had not been observed. They suggested that oestrogen was normally secreted by Sertoli cells, and that the high output of gonatrophins in the types with Sertoli-cell aplasia was due to the loss of the inhibitory effect of oestrogen upon the pituitary. Berthrong, Goodwin, and Scott (1949) have considered the secretion of oestrogen by Sertoli cells at some length, and have collected a good deal of evidence in favour of the hypothesis. They equate oestrogen with the "inhibin" of the older writers. So far no case intermediate between the Klinefelter and the Castillo type has been reported in the literature. The present case may well constitute a link, showing as it does gynaecomastia with relatively normal androgenic function and normal gonadotrophins. However, as testicular biopsy was refused there is no histological proof.

The physiology of mammary development is still imperfectly understood. Oestrogen and progesterone are undoubtedly important factors, but the position of the anterior pituitary is obscure. Turner (1944) and his school believe that mammary development is dependent upon two pituitary hormones, mammogen I and II; oestrogen and progesterone are thought to exert their action upon the mammary gland only through promoting the excretion of these pituitary principles. This hypothesis is not generally accepted.

The mechanism through which gynaecomastia appears in the testicular aplasias may now be considered. Overexcretion of oestrogen seems to have been excluded. Klinefelter, Riefenstein, and Albright, and Heller and Nelson found oestrogen secretion to be normal or low in all cases examined. Gynaecomastia occurs not in the type of case with intact Sertoli cells but in the types with aplasia of these cells and presumably a secretion of oestrogen lower than normal. Overproduction of anterior pituitary hormones would fit the facts better. Thus gynaecomastia occurs most commonly in the group described by Klinefelter *et al.*, in which gonadotrophin output is high, and so far has not been described in the group with normal gonado-

trophins. On the other hand, it fails to explain why gynaecomastia is much less common in the eunuchoid type and in castrates, in whom gonadotrophins again are high. The finding of more cases with normal gonadotrophins, like the one described here, would further disturb the hypothesis.

Dr. Raymond Greene suggested to me that the explanation of gynaecomastia should be sought in another direction: testicular aplasia is very likely due to a genetic disturbance. The same disturbance may in some cases also produce an increased susceptibility of the mammary tissues to normally circulating oestrogen. The idea has a good deal to recommend it.

Summary

A case of gynaecomastia is presented. Testicular aplasia is presumed. It is suggested that gynaecomastia in these cases may be due to a genetically determined over-sensitivity of the mammary tissue to normally circulating oestrogen.

My thanks are due to Mr. C. W. Hall for the photograph.

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BRACHIAL PLEXUS BLOCK

REPORT ON 350 CASES

BY

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Over a period of five years brachial plexus analgesia was administered for all operations on the upper limb when local analgesia was unsuitable. The patients were African or Bantu males aged between 18 and 65 employed on the Van Dyk Mine in the Transvaal. The operations varied from amputation through the middle of the humerus and the treatment of severe compound fractures of the upper arm and forearm to comparatively minor procedures on the fingers and hands. The cases will be divided into two series.

First Series (Various Techniques Used).—Total number of operations performed, 232. Perfect analgesia in 176, imperfect in 52, failures 4. The term "perfect" is used to indicate that no pain was felt; "imperfect" that the patient said he felt pain at some stage; and "failure" that the analgesic produced no appreciable effect. Imperfect results occurred with all analgesics used and with the six different techniques employed. The average amount injected of 1% or 2% procaine (or other analgesic of corresponding strength) was 36.5 ml. The reasons for the high percentage of imperfect results in this series were three: (1) Inexperience of the operator, who, trying different methods and analgesics, made no substantial improvement until the Macintosh and Mushin (1947) technique was employed and one drug—2% or 1% procaine, freshly prepared—was singled out for use. (2) The use of unsuitable, old, or too dilute analgesics. (3) Failure by the patients (all primitive Africans) to co-operate. The patient's co-operation is not required with the Macintosh and Mushin technique, which does not necessarily depend on subjective hyperaesthesia.