after a time in any event, but the oestrogen dosage may be halved or temporarily abandoned if desired. The further addition of progesterone does not appear to have any value in the treatment of gonadal dysgenesis.

Conclusions and Summary

A series of 27 patients with gonadal dysgenesis is presented. The absence of raised levels of urinary gonadotrophin excretion in this syndrome is shown to be a not uncommon finding. Cortisone was found not to reduce high excretions of gonadotrophin when these were present.

Attention is drawn to the comparatively infrequent occurrence of the classical congenital anomalies of "Turner's syndrome." Scepticism is expressed about the existence of cubitus valgus. Several patients in this series had good breast development when they were first seen. Biopsy in one untreated patient showed the breasts to consist of fat only. Tests of adrenocortical function displayed no impairment—even where sex hair was deficient. This tends to refute the view that the adrenal cortex alone governs axillary hair growth. Three cases are described in which moderate-to-severe osteoporosis occurred. This finding is discussed.

The presence of "ovarian stroma" and developing follicles on histological examination of the gonadal streaks is considered in relation to nuclear sexing of these patients. The anomalous finding of clitoral enlargement in "genetic" females is mentioned. Reference is made to patients who claim to have menstruated and to "normal-looking females" with gonadal dysgenesis.

The diagnosis of gonadal dysgenesis is discussed with particular reference to nuclear sexing. It is pointed out that this syndrome is probably the most common cause of primary amenorrhoea—whatever the appearance of the patient.

The treatment of gonadal dysgenesis is outlined.

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MORBIDITY FROM T.A.B.T. INOCULATION IN R.A.F. RECRUITS

BY

J. D. E. KNOX, M.B., Ch.B.
Late Squadron Leader, R.A.F.

AND

W. P. STAMM, F.R.C.P.
Air Commodore, Consultant in Pathology and Tropical Medicine to the Royal Air Force

Several clinicians at Royal Air Force schools of recruit training have gained the impression that a variety of morbid conditions, apart from immediate local and general reactions, may follow inoculation with T.A.B.T (a phenolized vaccine containing *Salmonella typhi, Salm paratyphi A* and *B*, and tetanus toxoid).

Robertson and Leonard (1956) stated that the conditions usually affected the joints and reticulo-endothelial system, and very occasionally seemed to initiate a cycle of events leading to a syndrome resembling the "collagen disorders." They suggested that infective conditions of all kinds, including upper respiratory infections, were more common during the seven to ten days following inoculation. They postulated that "all the immunological processes are disturbed at this time, giving rise to a general lowering of resistance to infection." These claims clearly called for a full investigation, for if they were substantiated the justification for routine inoculation of Service personnel would need careful reconsideration. This paper reports the results of such an investigation, carried out at five R.A.F. schools of recruit training over a period of one year. The opportunity was also taken to record the incidence of local and general reactions following inoculation.

Materials and Methods

At each of the five centres arrangements were made for recruits with even Service numbers to receive the usual doses of T.A.B.T. (0.5 ml. subcutaneously followed by 1 ml. four to six weeks later), and for those with odd numbers to be left uninoculated until arrival at their next unit. Both groups continued to be vaccinated against smallpox. Special records of sickness were kept on all recruits during their eight weeks of training, and a pathologist (J. D. E. K.) was

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appointed in overall charge of the arrangements at unit level. No special advice was given to the unit medical officers on matters of sterilization of syringes and needles, route and site of inoculation, etc., since the primary purpose of the trial was to establish whether there was any morbidity from T.A.B.T. inoculation as currently practised in the R.A.F. At the end of the experimental period the records were collected and analysed by the Medical Statistical Branch of the Air Ministry.

The numbers of recruits with even and odd numbers were 27,733 and 27,726 respectively, taking Royal Air Force and Women's Royal Air Force together. The actual number of recruits in the test group was 27,512, and 27,947 were in the control group. The difference in the size of the two groups from the "ideal" is accounted for as follows: 940 recruits who should have been in the test group were not given T.A.B.T. and 719 who should have been in the control group were given T.A.B.T. This results in a decrease in the number in the test group by 221, with a corresponding increase in the control group. It is thought that these errors were purely administrative and are unlikely to have biased the results.

Results

The overall incidence of sickness and the separate incidence of "diseases caused by infection," "accidents, poisoning, and violence," and "other diseases," are given in Table I. The total R.A.F. sickness rate of the test group

TABLE I.—*Incidence of Sickness in Control and Test Groups, R.A.F. and W.R.A.F.*

	R.A.F.				W.R.A.F.			
	Control		Test		Control		Test	
	No.	‰	No.	‰	No.	‰	No.	‰
Total No. at risk	27,063	—	26,680	—	884	—	832	—
Diseases caused by infection ..	7,876	291·0	7,471	280·0	252	285·1	189	227·2
Accidents, poisoning, and violence	2,768	102·3	2,622	98·3	105	118·8	85	102·2
Other diseases ..	5,352	197·8	5,331	199·8	332	375·5	225	270·4
Total ..	15,996	591·1	15,424	578·1	689	779·4	499	599·8

is significantly lower than that of the controls and this difference is most pronounced in the group "diseases caused by infection." Analysis of this latter group shows that it consists mainly of diseases of the upper respiratory tract, and in these the difference in incidence still persists (Table II).

TABLE II.—*Incidence of Upper Respiratory Infection in Control and Test Groups, R.A.F.*

Disease	Control		Test	
	No.	‰	No.	‰
Total No. at risk	27,063	—	26,680	—
Acute nasopharyngitis	1,915	70·5	1,845	69·5
Acute tonsillitis	778	28·7	647	24·2
Other acute upper respiratory infection	2,245	82·8	2,181	81·8
Influenza	237	8·8	223	8·4
Lobar pneumonia	40	1·5	36	1·3
Bronchopneumonia	37	1·4	36	1·3
Primary atypical, other, and unspecified pneumonia	118	4·4	117	4·4
Acute bronchitis	130	4·8	144	5·4
Bronchitis, chronic and unqualified ..	145	5·3	137	5·1
Total ..	5,645	209·0	5,366	201·0

In view of Robertson and Leonard's statement that reactions chiefly affected joints and the reticulo-endothelial system, a detailed analysis was made of diseases of bones and joints (Table III). It showed that there was no significant difference between the test and control groups. Diseases affecting the reticulo-endothelial system were too few for any valid statistical comparison, but the cases seen were equally distributed between the test and control groups.

TABLE III.—*Incidence of Diseases of Bone and Joints in Control and Test Groups, R.A.F.*

Disease	Control	Test
Total No. at risk	27,063	26,680
Arthritis	5	6
Muscular rheumatism	55	48
Rheumatism (unspecified)	4	9
Rheumatic fever	11	11
Other diseases of joints	53	35
Synovitis, bursitis, and tenosynovitis	216	235
Other diseases of muscles, tendons, and fascia	4	3
Diseases of the bones	4	6
Curvature of the spine	36	41
Flat-foot	100	98
Other deformities	95	98
Total	583	590
Total incidence per 1,000	21·6	22·2

TABLE IV.—*Immediate Local and General Reactions to T.A.B.T. at Each Centre, R.A.F.*

Centre	No. at Risk	Percentages Affected					
		Local Reaction			Local and General Reaction		
		Negligible	Considerable	Admitted or Detained	Slight	Considerable	Admitted or Detained
1	6,305	97·06	1·38	0·03	0·24	0·10	1·19
2	4,453	97·62	1·10	0·04	0·52	0·20	0·52
3	2,479	96·37	1·49	0·08	0·65	0·24	1·17
4	8,600	96·69	2·34	0·03	0·38	0·14	0·42
5	4,843	97·03	1·32	0·10	0·27	0·06	1·22
Total:	26,680	96·96	1·64	0·05	0·38	0·14	0·83

The immediate reactions, both local and general, to the inoculations were recorded, and are summarized in Table IV; the incidence of recruits rendered temporarily unfit for duty and requiring admission to sick quarters was approximately 1%.

A number of medical officers gave the majority of their inoculations intramuscularly, but no difference could be detected between the immediate local and general reactions to these injections and those following subcutaneous inoculation.

Because of the possibility that T.A.B.T. might contain "A" substance (Crawford *et al.*, 1952) an analysis of reactions to T.A.B.T. by blood groups was carried out at one of the centres on those subjects whose blood group was known. The results (Table V) show no significant difference between persons of different blood groups.

TABLE V.—*Immediate Local and General Reactions to T.A.B.T. by Blood Groups*

Blood Group	No. at Risk	Percentages Affected					
		Local Reaction to T.A.B.T.			Local and General Reaction to T.A.B.T.		
		Negligible	Considerable	Admitted or Detained	Slight	Considerable	Admitted or Detained
AB	82	98·78	0·00	0·00	0·00	0·00	1·22
A	913	98·02	0·88	0·00	0·22	0·00	0·88
B	189	96·82	1·06	0·00	0·53	0·53	1·06
O	976	98·05	1·03	0·10	0·10	0·00	0·72
Rhesus +	1,826	98·03	0·88	0·05	0·22	0·05	0·77
Rhesus −	334	97·60	1·20	0·00	0·00	0·00	1·20
Total:	2,160	97·96	0·93	0·05	0·18	0·05	0·83

During the investigation the opportunity was taken to inquire into the relationship between T.A.B.T. inoculation, smallpox vaccination, and false-positive serological tests for syphilis. The results, details of which have already been reported by Mason and Headland (1955), showed that smallpox vaccination may give rise to 2% false-positive Kahn reactions but that T.A.B.T. had no such effect.

No cases of peripheral neuritis were seen, such as were described by Miller and Stanton (1954). There were two cases of acute encephalitis, both in the control group; two cases of poliomyelitis, one in each group; and four cases of meningitis, two in each group.

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Discussion

The results of this investigation do not support some of the impressions recorded by Robertson and Leonard. The present results do not exclude the possibility of individual rare syndromes, such as the single cases of "collagen disease" reported by these authors, being caused by T.A.B.T. inoculation.

That unit medical officers were all too ready to ascribe miscellaneous morbid conditions to inoculation was exemplified by occasional cases of traumatic synovitis belonging to the control group being labelled "T.A.B.T. arthropathy." It appeared that many junior medical officers had been warned by their professional seniors of the important aetiological role of T.A.B.T. in what Ogilvie (1954) terms "ephebiatrics."

It should be remembered that T.A.B.T. is usually given at a time when the recruit is adapting himself to a new environment, and that the immediate post-inoculation period is the time when his reaction to "herd life" may be expected to become apparent.

Although the admission of 1% to sick quarters following T.A.B.T. inoculation seems reasonably small at first sight, it can cause considerable administrative embarrassment when large numbers are involved. This admission rate, however, was less than that due to vaccination (1.5%).

Summary

A survey was carried out on 55,459 R.A.F. and W.R.A.F. recruits to determine the morbidity following T.A.B.T. inoculation. The incidence of disease in the test group was significantly lower than that in the controls; nearly all this difference was accounted for by "diseases caused by infection" and persisted in "diseases of the upper respiratory tract."

The admission rate to sick quarters following T.A.B.T. inoculation was 1%, and following smallpox vaccination 1.5%.

No difference in immediate local and general reactions could be detected between subcutaneous and intramuscular T.A.B.T. inoculation.

There was no significant difference between the reactions to T.A.B.T. inoculation classified according to the blood groups of the patients.

T.A.B.T. does not appear to give rise to false-positive Kahn reactions, but vaccination may cause up to 2% false-positive results.

No cases of peripheral neuritis were seen.

We thank the Medical Statistical Branch of the Air Ministry for their willing assistance, and particularly Mr. E. W. N. Ratcliff, who carried out most of the statistical analyses. We also thank the Principal Medical Officer of Technical Training Command and the numerous medical officers, administrative officers, and airmen, without whose co-operation this investigation could not have been completed. We are indebted to the Director-General of Medical Services for permission to publish this paper.

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Since the second world war 976 new homes for the aged had been opened in England and Wales, said the Minister of Health, Mr. DEREK WALKER-SMITH, Q.C., when opening an L.C.C. home for the elderly this month. Referring to the size of the problem in Britain, he said that to-day one person in nine was over 65, compared with one in 21 at the beginning of the century. By 1975 this proportion would have risen to one in seven.

MEGALOBLASTIC ANAEMIA OF INFANCY TREATED WITH FOLIC ACID

BY

FRANK WALT, M.R.C.S., D.C.H.
Consultant Visiting Paediatrician, Paediatric Department, McCord Zulu Hospital, Durban

S. HOLMAN, M.D., B.Sc., D.C.P.
Late Senior Lecturer in Pathology, Durban Medical School; Late Clinical Pathologist, King Edward VIII Hospital, Durban

AND

P. NAIDOO, M.B., B.Ch.
Late Registrar, Paediatric Department, McCord Zulu Hospital, Durban

Megaloblastic anaemia in infants was thought to be rare at the McCord Zulu Hospital, Durban, until an incidence of 5.4% was found in 1954 (Walt *et al.*, 1956). Diagnosis was made by bone-marrow examination alone, patients for aspiration being chosen on clinical grounds or when the haemoglobin was below 6.7 g./100 ml. Because that investigation left many questions unanswered a controlled project was initiated. The objectives were to find the true incidence of megaloblastosis; the significance of reticulocytosis; the rapidity with which the bone marrows returned to normal; the part played by antibiotics, particularly penicillin; the cause of the sudden drop in haemoglobin or "crisis" in some patients; and the reasons for the development of megaloblastosis. Answers to some of these questions can now be given.

Although it has been known for a long time that folic acid will cure the megaloblastosis and therefore a deficiency of folic acid is presupposed, we still do not know whether the deficiency is due to lack of intake, absorption, or utilization, nor why it is commonest amongst our cases of kwashiorkor.

Material and Methods

These were similar to those described previously (Walt *et al.*, 1956). To determine the incidence of megaloblastic anaemia in this hospital the bone marrow of every case admitted to the children's wards was aspirated within 24 hours of admission. The series ran from February 14, 1955, to June 5, 1955 (excluding 23 days between March 22 and April 13 because of the Easter vacation), during which time 217 cases were admitted. The bone marrows of 201 cases were examined; of the 16 cases not aspirated, 6 were omitted in error and 10 patients died within a few hours of admission, post-mortem specimens not being obtained.

A further objective was to determine whether the reticulocyte response was a satisfactory measure of effective therapy with folic acid and whether a particular pattern of reticulocyte response could be observed. Two groups of patients were therefore chosen, the first comprising all cases with megaloblastic anaemia and the second consisting of non-megaloblastic cases taken entirely at random; this was done arbitrarily by using every fifth patient admitted as a control case. If the fifth patient suffered from megaloblastic anaemia the next non-megaloblastic case was placed in the control group. This series yielded 18 cases of megaloblastic anaemia and 31 control cases (non-megaloblastic).

The two groups were treated in exactly the same manner, each being given 5 mg. of folic acid three times a day, followed by re-aspiration of the bone marrow within 96 hours. Reticulocyte estimations by the method of Dacie

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