BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 6 1962

HEREDITY IN COMMON DISEASES

A RETROSPECTIVE SURVEY OF TWINS IN A HOSPITAL POPULATION

BY

A. G. MARSHALL,* M.A., M.D. ELSPETH O. HUTCHINSON, B.A.

AND

JILLIAN HONISETT, B.Sc.

The Royal Hospital, Wolverhampton

In a discussion on the importance of genetic factors in the common diseases of mankind, Burnet (1953) advocated the usefulness of the twin-study method. He expressed his anxiety at the genetic deterioration in modern society and his belief in the importance of widespread knowledge of the pattern of inheritance in common conditions as well as in the rare and striking human genetic anomalies.

It was therefore decided to investigate the feasibility of applying this method to the patients attending a busy general hospital. The rationale of twin study in the investigation of heredity in disease has been discussed by many other authors besides Burnet (Gates, 1952; Waterhouse, 1953; Doig and Pitman, 1957; Carter, 1957). It seems sufficient in this paper to state that identical or monozygotic (M.Z.) twins would be expected to have exactly the same inherited traits as each other, while fraternal or dizygotic (D.Z.) twins would resemble one another, in this respect, no more than other siblings. In each case the environment in childhood would be expected to be as nearly the same in each of a pair as can be achieved in human society without special and artificial methods.

Twin studies are therefore useful in the investigation of the origins of disease, for if a disease is found to occur more commonly in both of an M.Z. twin pair than it does in both of a D.Z. pair, it may be concluded that there is some inherited factor. Even when this is so, it is usually necessary for various environmental conditions to be present as well before the disease becomes manifest.

Such studies, of course, are not designed to determine if any disease occurs more often in twins than in singletons, but simply to compare its incidence in both members of identical and fraternal twins.

Three factors are of primary importance in such a survey, and they all present difficulties. Firstly, accuracy in distinguishing M.Z. from D.Z. twins; secondly, accuracy in retrospective diagnosis of disease; and, thirdly, the collection of large numbers for the purpose of statistical analysis, which helps to counteract the effects of such inaccuracies as are bound to creep into a study based largely on human memory and veracity. It is, of course, important to exclude bias in selection of material.

*In receipt of a grant from the Birmingham Regional Hospital Board.

Method

The twins were found by direct interview of the out-patient population of the hospital. One of us (E. O. H., then J. H.) asked each patient attending the hospitals of the Wolverhampton Group if they were twins, or knew any twins well. Histories were taken on the spot if possible, or, if not, the twins were interviewed or visited as soon as practicable. When large clinics were held in two separate hospitals at the same time, simple questionaries were distributed to the out-patients by the sisters and co-operation by the twins was most encouraging; they were interviewed later. A few pairs were found in the casualty department, and some who had not passed through the out-patient departments were notified to us by the ward sisters. Those attending the radiotherapy department were not included.

At a later stage an attempt was made to find another series of twins by the use of the local records of the medical officer of health, but this resulted in finding only a series of healthy infants, and none of them was included in our series.

After collecting for two years in Wolverhampton, when about 1,550 pairs had been found, it began to appear that the supply of twins was becoming exhausted, so that more and more of them were found to have been interviewed before. It became necessary to explore new fields, and the inquiry was extended to the General Hospital, Birmingham.

As soon as possible after the initial record had been completed, it was carefully reviewed in each case, using all the hospital notes and when necessary by speaking to the general practitioners concerned. More information was sometimes sought by letter and in some cases the twins were seen again. Finally all the items of the record were coded; punched cards were prepared and machine-sorted to classify the results.

No healthy twins were included in the collection, nor were infants under 2 years of age. When one twin was stillborn or died in infancy the pair was omitted, but, apart from this, all the pairs were included as they were encountered. Only in the few cases where it proved impossible to verify the medical history was the pair left out of the total. Each interview was conducted from a standard questionary, so that in every case the same questions were asked.

Besides the birth status and personal details, inquiries were made about other twins in the family and the

mother's age. Very careful inquiry was made to decide whether the twins were fraternal or identical; much weight was placed on the opinion of near relatives and friends, especially in easy recognition of one from the other. For example, in one identical pair, their own children sometimes mistook father for uncle. The medical history was equally carefully investigated, using evidence from the family and friends for each member of the pair separately, and the co-twin was investigated in the same way.

Ovularity

In order to check the accuracy of our diagnosis of identical and fraternal status, it was originally intended to determine the blood groups and subgroups of a large proportion of the twins. Since there is a shortage of the necessary grouping sera the number had to be small, but the main factor in our failure to achieve adequate data in this respect was unwillingness on the part of the twins themselves. So many of them defaulted that the scheme had to be abandoned.

However, the check was made on 44 pairs, and in 36 of them our opinion proved to be correct ($P<0.001$) (Table I). Race and Sanger (1954) state that the use of all the available antisera gives a probability of about 97% in the diagnosis of M.Z. twins, but Kallmann and Reisner (1943) regard personal inspection and family evidence as the best method of distinguishing the two types.

TABLE I.—*Check on Ovularity by Blood Group in 44 Pairs*

	Thought to be Monozygotic	Thought to be Dizygotic	Total
Shown to be monozygotic	25	3	28
,, ,, ,, dizygotic ..	5	11	16
Total	30	14	44

$\chi^2 = 13{\cdot}25$. $P<0{\cdot}001$.

Diseases

The acute infectious diseases of childhood were excluded because we found a good deal of confusion and the diagnosis could seldom be checked. Likewise diphtheria, which seemed to have such a high incidence that it was surely confused with other throat infections. Nasal sinusitis was included only if a surgical operation such as paracentesis had been performed, and otitis media was diagnosed only if there had been an aural discharge or surgical operation. In regard to the common "bad chest" we had to compromise with either (1) pneumonia admitted to hospital or other satisfactory evidence or (2) chest trouble severe enough to entail absence from work for more than a week in two or more consecutive winters. We call this "chest infection." Batty Shaw and Fry (1955) state that the main clinical distinction between bronchitis and pneumonia is the degree of constitutional disturbance.

We were also in difficulty in the diagnosis of squint, which seems to be a term of approbation in this part of the world; finally we had to include with it all visual defects starting in childhood which could not be otherwise explained. In the diagnosis of infective hepatitis every effort was made to exclude other causes of jaundice. Finally, our term "rheumatism" includes all kinds of chronic or recurrent arthritis, mainly because it was so often impossible to make a more accurate diagnosis.

A simple code was used, based on the anatomical site and pathological process involved.

General Results

With due regard to all these factors, our final collection numbered 2,537 pairs of twins, 1,722 of them found in Wolverhampton and a supplement of 815 in Birmingham. Eight sets of triplets were encountered.

We regarded 705 pairs as identical twins and 1,832 pairs as fraternal, a proportion of 27.8% and 72.2%. Table II shows their distribution; the percentages of like and unlike sexes have been calculated for comparison

TABLE II.—*Distribution of Twin Pairs by Sex*

	Wolverhampton	Birmingham	Total
M.Z. ♂♂ ..	214 } 27·7%	91 } 27·7%	305 } 705 (27·8%)
♀♀ ..	264 }	136 }	400 }
D.Z. ♂♂ ..	283	143	426 }
♀♀ ..	349	155	504 } 1,832 (72·2%)
♂♀ ..	612	290	902 }
Total ..	1,722	815	2,537

Total	Ratio	♂♂ : ♀♀ : ♂♀
♂♂ 731 = 28·8%	Wolverhampton	1 : 1·23 : 1·23
♀♀ 904 = 35·6%	Birmingham	1 : 1·24 : 1·24
♂♀ 902 = 35·5%	Total	1 : 1·23 : 1·23

TABLE III.—*Distribution of Twin Pairs by Age, Sex, and Ovularity*

Age in Years	♂♂		♀♀		♂♀		M.Z. ♂		M.Z. ♀		All M.Z.		D.Z. ♂		D.Z. ♀		All D.Z. Like Sex		D.Z. ♂♀		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
2–9	165	22·5	153	16·9	190	21·2	74	24·2	84	21	158	22·4	91	21·4	69	13·7	160	17·2	190	21·2	508	20
10–19	157	21·4	200	22·1	185	20·1	60	19·7	96	24	156	22·1	97	22·8	104	20·6	201	21·6	185	20·1	542	21·3
20–29	134	18·3	151	16·7	133	14·7	54	17·7	73	18·5	127	18	80	18·7	78	15·5	158	17	133	14·7	418	16·5
30–39	118	16·2	167	18·5	147	16·4	52	17	57	14·5	109	15·5	66	15·5	110	21·8	176	19	147	16·4	432	17
40–49	83	11·4	111	12·8	122	13·5	38	12·4	35	8·8	73	10·4	45	10·5	76	15·1	121	13	122	13·5	316	12·4
50–59	40	5·5	70	7·7	76	8·4	16	5·2	33	8·3	49	7	24	5·6	37	7·4	61	6·3	76	8·4	186	7·3
60–69	23	3·1	29	3·2	24	2·7	6	1·9	11	2·7	17	2·4	17	4	18	3·6	35	3·8	24	2·7	76	3
70+	11	1·5	23	2·5	25	2·8	5	1·6	11	2·7	16	2·3	6	1·4	12	2·4	18	1·9	25	2·8	59	2·3
Total	731	100	904	100	902	100	305	100	400	100	705	100	426	100	504	100	930	100	902	100	2,537	100

TABLE V.—*Distribution of 2,352 Pairs of Twins According to Mother's Age at their Birth*

	Mother's Age (Years)																Total
	–19		20–24		25–29		30–34		35–39		40–44		45–49		50+		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
M.Z. ♂♂ ..	7	2·5	53	19·2	72	26·1	82	29·8	49	17·8	11	3·9	2	0·7	0	—	276
M.Z. ♀♀ ..	7	1·9	69	18·3	124	32·8	88	23·1	70	18·5	17	4·5	3	0·8	0	—	378
D.Z. ♂♂ ..	3	0·7	57	14·6	102	26·2	112	28·8	81	20·4	28	7·2	6	1·5	0	—	389
D.Z. ♀♀ ..	5	0·1	65	1·4	122	26·1	137	29·3	100	21·4	33	0·7	5	0·1	0	—	467
D.Z. ♂♀ ..	3	0·4	107	12·7	250	29·7	231	27·4	183	21·8	58	6·9	8	1·0	2	0·2	842

with the figures given by Waterhouse (1950). There is a slight but appreciable difference, which is least marked in the proportion of males. Our figures are closer to the proportions which he quotes from the Registrar-General's returns of the distribution at birth, and they are quite consistent with Newman's (1917) figures, although our collection was derived from a special population of hospital patients. Gates (1952) states that 25–28% of Caucasian twins are monozygotic, but he also refers to a somewhat higher proportion from other sources. Weinberg's method applied to our figures gives a total of 658 M.Z. pairs, but this method assumes an equal sex ratio at birth. There is no significant difference between the Wolverhampton and Birmingham components of our collection in this respect, and we think that the results shown in Table II support our view that our material is surprisingly free from selection.

In Table III the collection is classified in age-groups, and the first part of it can be compared with Table V of Waterhouse (1950). He draws attention to the steady decline in the proportion of M.M. pairs with advancing age and a compensatory rise in the F.F. pairs. In the first two decades he found an excess of males, and our results are broadly the same. In the age-group 20–29 years, however, our figures show an excess of M.M over F.F. pairs and differ significantly from Waterhouse's proportions ($P<0.01$). It will be noted that this does not apply to the M.Z. twins, but it is present in the D.Z. pairs. In subsequent decades this male preponderance is lost except in the case of M.Z. twins in the fourth and fifth decades, and in these our figures also differ significantly from Waterhouse ($P<0.001$). It seems, therefore, that the higher proportion of M.M. pairs is now prolonged into the third decade and that in the case of M.Z. twins it persists into the fourth and fifth decades. This is the only respect in which our Birmingham and Wolverhampton materials differ significantly from each other, for in the former this later male preponderance in M.Z. twins does not appear (Table IV). As the numbers in these two groups are so different, however, we do not place much emphasis on this deviation, but it is tempting to remember that the majority of Waterhouse's twins probably came from Birmingham. It would be pleasing to think that this apparent improvement in survival of males is a result of better social conditions over the last 30 years or so.

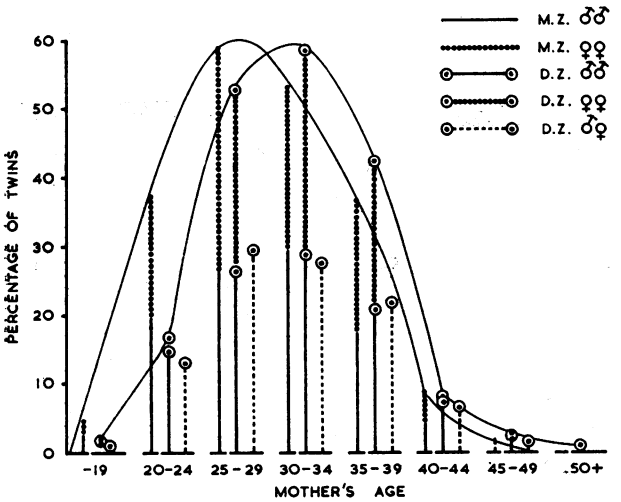

Chart showing percentage of twins of each category born to mothers of each age-group.

It is generally believed that identical twins die out more rapidly than fraternal ones, and we have tried to extract information on this point from Table III. A smaller proportion of M.Z. pairs are alive after the age of 40 years than the same proportion of D.Z. pairs (including mixed sexes) ($0.02<P<0.05$), but this is not so if only like-sex pairs are considered. The significance of this difference is greatly increased if the age is reduced to 30 years ($0.001<P<0.01$), suggesting that the maximum differential mortality occurs in the first 30 years of life, and at this age the same significant difference is found for like-sex pairs as well.

Table V shows the distribution of our cases according to the mother's age at their birth, and the total is smaller than our grand total because this information was not known to some of the twins. The Chart shows diagrammatically the percentage of twins of each category born to mothers of each age-group, and there are two peaks — for M.Z. pairs at 25–29 years and for D.Z. pairs at 30–35 years. If the numbers of twins born to mothers above and below 30 years of age are compared there is a significant difference between M.Z. and D.Z. like-sex pairs ($P<0.001$) and also between M.Z. and D.Z., including unlike-sex pairs ($0.001<P<0.01$). It seems from the Chart that the peak for male identicals is somewhat later than that for all identicals, but tests of significance are equivocal. However, in interpreting these findings it must

TABLE IV.—*Comparison of Birmingham and Wolverhampton Series*

Age-group	All ♂♂				All ♀♀				M.Z. ♂♂				M.Z. ♀♀				D.Z. ♂♂				D.Z. ♀♀				D.Z. ♂♀			
	Wolv.		Birm.		Wolv.		Birm.		Wolv.		Birm.		Wolv.		Birm.		Wolv.		Birm.		Wolv.		Birm.		Wolv.		Birm.	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
2–9	122	24·8	43	18·4	106	17·6	47	16·2	54	25·1	20	22	58	22	26	19·1	68	24	23	16·1	48	13·8	21	13·5	138	22·5	52	17·9
10–19	90	18·1	67	28·6	126	22·8	74	25·2	33	15·4	27	29·7	60	22·7	36	25·8	57	20	40	28	66	18·9	38	24·5	104	17	81	26·9
20–29	92	18·5	42	17·9	97	15·8	54	18·5	37	17·3	17	18·7	44	16·7	29	21·3	55	19·4	25	17·5	53	15·2	25	16·1	89	14·5	44	15·2
30–39	84	16·8	34	14·1	121	19·7	46	15·8	39	18·2	13	14·3	36	13·6	21	15·5	45	15·9	21	14·7	85	24·4	25	16·1	108	17·6	39	13·5
40–49	63	12·7	20	8·6	78	12·7	33	11·3	33	15·4	5	5·5	24	9·2	11	8·1	30	10·6	15	10·5	54	15·5	22	14·2	88	14·4	34	11·7
50–59	25	5	15	6·4	47	7·7	23	7·9	11	5·1	5	5·5	25	9·4	8	5·8	14	4·9	10	7	22	6·3	15	9·7	53	8·7	23	7·9
60–69	16	3·2	7	3·0	21	3·4	8	2·8	5	2·3	1	1·1	8	3·1	3	2·1	11	3·9	6	4·2	13	3·7	5	3·2	18	2·9	6	2·1
70+	5	1·1	6	2·6	17	2·8	6	2·1	2	0·9	3	3·3	9	3·4	2	1·4	3	1·1	3	5·6	8	2·3	4	2·6	14	2·3	11	3·8
Total	497		234		613		291		214		91		264		136		283		143		349		155		612		290	

TABLE VI.—*Incidence of Common Diseases in the Twins*

Disease	No. of Twin Pairs					Incidence of Disease														
	M.Z.		D.Z.			Excluding Mixed Dizygous							Including Mixed Dizygous							
						M.Z.		D.Z.					M.Z.		D.Z.					
	M.	F.	M.	F.	Mixed	% Concordant	% Discordant	% Concordant	% Discordant	t	P	Significance	% Concordant	% Discordant	% Concordant	% Discordant	t	P	Significance
Appendicitis	38	62	63	78	99	16·3	83·7	6·8	73·2	2·17	0·05–0·02	S	16·3	83·7	6·7	93·3	2·6	0·01–0·001	S
Asthma	7	3	8	5	13	11·0	89·0	0	100·0	1·22		NS	11·0	89·0	0	100·0	1·69	0·1–0·05	NS
Benign tumour	30	66	28	87	89	20·0	80·0	12·7	87·3	1·33		NS	20·0	80·0	10·5	89·5	2·1	0·05–0·02	S
Chest infection	163	184	196	195	399	36·3	63·7	19·9	80·1	4·3	<0·001	S	36·3	63·7	21·5	78·5	4·5	<0·001	S
Otitis media	54	80	70	76	132	30·1	69·9	9·8	90·2	4·0		S	30·1	69·9	10·8	89·2	4·46	<0·001	S
Eczematous dermatitis	11	7	2	16	36	28·6	71·4	8·0	92·0	5·15		S	28·6	71·4	8·6	91·4	2·03	0·05–0·02	S
Epilepsy	21	38	24	32	58	37·2	62·8	1·8	98·2	4·6	<0·001	S	37·2	62·8	3·6	96·4	5·55	<0·001	S
Fibrositis	6	4	2	9	14	25·0	75·0	11·1	88·9	0·75		NS	25·0	75·0	9·9	90·1	1·13		NS
Fractures	70	59	97	54	166	15·2	84·8	11·9	88·1	0·66		NS	15·2	84·8	11·2	88·8	1·09		NS
Hernia	46	14	54	7	67	25·0	75·0	10·9	89·1	1·88	0·1–0·05	NS	25·0	75·0	8·5	91·5	2·46	0·02–0·01	S
Hypertension	4	10	4	14	19	27·3	72·7	5·9	94·1	1·6		NS	27·3	72·7	15·6	84·4	0·86		NS
Infective hepatitis	8	24	11	15	27	45·5	54·5	18·2	81·8	1·94	0·1–0·05	NS	45·5	54·5	17·8	82·2	2·45	0·02–0·01	S
Malignant growth	4	9	7	12	18	0	100·0	0	100·0				0	100·0	0	100·0			
Peptic ulcer	20	4	26	8	25	14·3	85·7	6·3	93·7	0·97		NS	14·3	85·7	3·5	96·2	1·73	0·1–0·05	NS
Piles	9	1	8	12	19	11·1	88·9	11·1	88·9				11·1	88·9	14·7	85·3	0·28		NS
Psoriasis	1	9	4	4	6	11·1	88·9	13·3	86·7	0·13		NS	11·1	88·9	7·7	92·3	0·28		NS
Psychoneurosis	4	5	5	4	15	14·3	85·7	0	100·0	1·25		NS	14·3	85·7	4·5	95·5	0·97		NS
Rheumatism	24	39	24	50	101	26·0	74·0	10·5	89·5	2·2	0·05–0·02	S	26·0	74·0	8·7	91·3	3·2	0·01–0·001	S
Sinusitis	19	20	21	24	49	34·5	65·5	12·5	87·5	2·18	0·05–0·02	S	34·5	65·5	13·3	86·7	2·5	0·02–0·01	S
Skin infections	25	33	50	31	60	20·8	79·2	14·1	85·9	1·19		NS	20·8	79·2	10·2	89·8	1·86		NS
Squint	47	72	64	78	120	41·8	58·2	19·3	80·7	3·57		S	41·8	58·2	18·1	81·9	4·57	<0·001	S
Pulmonary tuberculosis	9	20	13	53	56	7·4	92·6	4·8	95·2	0·49		NS	7·4	92·6	8·0	92·0	0·1		NS
Urinary infection	4	4	1	11	11	14·3	85·7	20·0	80·0	0·3		NS	14·3	85·7	9·5	90·5	0·65		NS
Varicose veins	22	30	13	66	76	30·0	70·0	12·9	87·1	2·2	0·05–0·02	S	30·0	70·0	9·2	90·8	3·38	<0·001	S

be remembered that no account has been paid to the natural distribution of all births in respect to the mother's age, and our conclusions are therefore open to criticism. So far as they go, they tend to support previous evidence that identical twins are born of younger mothers than fraternal twins (Waterhouse, 1950).

We had hoped to be able to produce some information about other twins in the families of our pairs, but the information at our disposal appears to be too unreliable. It must be remembered that we are not dealing with volunteers in the same sense as Waterhouse, and some of our subjects were unwilling to take the trouble to check such information for us.

Pathological Conditions

Our findings in respect of past illnesses are summarized in Table VI, where the number of twins of each category giving a history of the disease is stated in the form of concordance and discordance. A statistical analysis is shown, firstly limited to like-sex pairs and then for the total number by including unlike-sex pairs as well. There is, of course, nothing in these results which gives any information about the liability of twins to develop a disease on account of their twin-status.

It is generally believed that a significant difference between the relative proportions of M.Z. and D.Z. pairs concordant for any pathological condition indicates a hereditary factor (Waterhouse, 1953). For the sake of brevity this situation will hereafter be described as "significant" and the contrary as "not significant."

Comparison in this way is usually confined to like-sex pairs in order to obviate any bias due to sex. From Table VI it will be seen that inclusion of unlike-sex twins has altered the significance in only three conditions—namely, benign growth, hernia, and infective hepatitis. It will also be seen that there is wide variation in the total numbers in each disease, and this of course must affect the reliability of some of our findings. In no case was a significant difference found when the total number in any condition was below 80, and in two diseases (eczematous dermatitis and infective hepatitis), although a significant difference was observed, the total numbers are only of this order. It is quite likely that larger total numbers might alter the interpretation to be placed on the results for asthma, fibrositis, hypertension, malignant growth, piles, psoriasis, psychoneurosis, and urinary infection, but we can do no more than report our actual findings. We think it likely that, when the total numbers in any disease are considerably greater, a not-significant result may be taken to indicate the absence of any hereditary factor detectable by this method.

Many diseases other than those in Table VI were included in our inquiry, but they have been omitted because the total numbers were too small for analysis.

We found a significant difference in exactly half of the 24 diseases shown in this Table—namely, appendicitis, benign growth, chest infections, otitis media, eczematous dermatitis, epilepsy, hernia, infective hepatitis, rheumatism, sinusitis, squint, and varicose veins. In 8 of the remaining 12 the numbers are below 80 and no conclusions may be drawn. The remaining four which are not significant are fractures, peptic ulcers, skin infections (recurrent boils, impetigo, etc.), and

tuberculosis. Unfortunately we did not subdivide our cases of fracture according to causation (carelessness on the part of the subject, etc.), so the figures have no value as an estimate of accident proneness. The total numbers in peptic ulcer are borderline, but in the case of skin infection and tuberculosis the numbers appear to be adequate.

Of the 12 diseases in which significant results suggest some hereditary factor, five are due to infections—namely, appendicitis, chest infections, otitis media, infective hepatitis, and sinusitis. In three there is some functional defect probably arising from an anatomical abnormality—that is, hernia, squint, and varicose veins. Benign growth includes angioma, lipoma, and adenoma of any organ, but it could not be subdivided as the numbers would thereby be reduced too much for analysis. Eczematous dermatitis includes adults as well as children, and epilepsy includes petit mal. As described above, it was found impossible to differentiate the various kinds of arthritic diseases, and the rheumatism group includes all chronic affections of the joints except gout.

Discussion

Harvald and Hauge (1956) reported on 1,900 pairs of Danish twins and promised a further report, but we have been unable to trace it. They are broadly in agreement with our findings in peptic ulcer and tuberculosis but differ from us about rheumatism. They state that the paper by Camerer and Schleicher (1935), concerning 1,500 twins, is confined to isolated diseases in childhood; that paper is not available in this country (P. Wade, 1961, personal communication). Doig and Pitman (1957) found a general lack of genetic factors in appendicitis and fractures, while Doig (1957) confined his investigation to duodenal ulcer, agreeing with our results in peptic ulcer (*Brit. med. J.*, 1958). Siemens (1924), reporting on small numbers, agrees with us on otitis media and squint but disagrees about appendicitis. Gebbing (1936) agrees with us in regard to otitis media, appendicitis, and tuberculosis in children.

Space does not allow a comparison of our results with more general studies of genetics, but the latter are in agreement with us except in infective hepatitis, peptic ulcer, and tuberculosis (but see Hanhart, 1953).

The hereditary factor which we believe to be shown by our "significant difference" might operate through an anatomical or physiological inferiority of the affected organ—for example, the persistent sac in hernia or the enzyme deficit in goitre (Stanbury, 1960). Gebbing (1936) suggests an inherited failure of specific antibody production, and Moncrieff (1953) describes such family traits, while both Gates (1952) and Sorsby (1953) discuss this hypothesis at length and give many references. Apart from gross congenital defects, we think that in general it is necessary for an environmental agent to act in conjunction with the inherited factor before the disease becomes manifest (Lawrence, 1955; *British Medical Journal*, 1956; D. D. Reid, 1958; Oswald, 1958; L. Reid, 1958; Karlish and Tarnoky, 1960). As Woodworth (1941) puts it, both fuel and oxygen are necessary for making a fire.

Most of the conditions in Table VI that are due to infection appear to be associated with a hereditary trait and could result from an inherited disturbance of antibody production. The organ specificity, however, throws some doubt on this, and Marshall (1953, 1956) suggested that minor structural defects in the kidney, consequent on failure of full vascular differentiation, rendered it liable to infection. Such a hypothesis might apply to other organs.

Two of our findings are worth further comment. Our results in infective hepatitis are not conclusive, but they are suggestive enough to warrant further study (Debré, 1939; Parsons, 1939; Dible *et al.*, 1954; Singh *et al.*, 1961). We cannot explain our findings in tuberculosis nor why this type of infection should not follow the pattern of susceptibility in other chest infections.

In conclusion, we feel that much more could have been gained if it had been possible to add a more complete study of family and environment. Burnet (1953) recommends the establishment of a permanent twin research department in all major teaching hospitals and our experience leads us to support his suggestion so that more complete and continuous studies could be made. Although most of our findings are amply supported in the literature, we hope that our paper may arouse a wider interest in this aspect of common diseases.

Summary

A total of 2,537 pairs of twins have been discovered among hospital patients: 1,725 pairs were found in the hospitals of the Wolverhampton Group and 812 pairs in the General Hospital, Birmingham.

The twins were divided into identical and fraternal pairs by personal inspection and questioning and by family opinion.

The sex ratios and the proportions of identical and fraternal pairs were compared with a previous collection of twins from the same district. Analysis of these factors confirms that this series is reasonably free from bias.

There is some evidence to suggest that the previously reported increased mortality of males compared with females is less marked than before.

Retrospective medical histories were taken individually from the whole collection. After scrutiny and checking these histories were classified and the results analysed.

The incidence of 24 common diseases in this series was examined by the method of concordance and discordance. In eight such diseases the numbers were insufficient for analysis.

In 12 diseases there is evidence of a hereditary factor; the strength of this evidence varies. They are appendicitis, benign growth, chest infections, otitis media, eczematous dermatitis, epilepsy, hernia, infective hepatitis, rheumatism, sinusitis, squint, and varicose veins. In all but one of them there are already records to suggest an inherited trait. The exception is infective hepatitis. While our evidence is somewhat tenuous it is suggestive of a genetic factor in susceptibility to this disease.

In the remaining four conditions our results suggest that there is no genetic background, and they are in accordance with previously published work except in one instance. The exception is pulmonary tuberculosis. Comment is made on its different background from recurrent chest infections, in which our results show clearly that there is an inherited factor, and on the fact that our findings differ from those of previous investigators.

From our experience in making this survey we support Burnet's (1953) suggestion for the establishment of permanent twin research departments in certain centres.

This work was supported by a Research Grant made by the Birmingham Regional Hospital Board, to whom we express our gratitude.

Our thanks are due to the clinical staff of the Wolverhampton Group of Hospitals and of the General Hospital, Birmingham, as well as to the many general practitioners and consultants who have so generously helped us. We also thank the nursing staff and the administrative officers of these and many other hospitals in the district. Dr. Dorothy Parkin kindly undertook the serological typing, and Dr. J. A. H. Waterhouse with his staff has given us much help and encouragement. Dr. J. Galloway and Dr. W. Weiner kindly helped us with records from their departments. We also thank the twins and their families for their patience and co-operation.

REFERENCES

Batty Shaw, A., and Fry, J. (1955). *Brit. med. J.*, **2**, 1577.
Brit. med. J., 1956, **1**, 906.
—— (1958). **1**, 1470.
Burnet, M. (1953). *Lancet*, **1**, 104.
Camerer, J. W., and Schleicher, R. (1935). Quoted by Harvald and Hauge (1956).
Carter, C. O. (1957). *Brit. med. J.*, **2**, 1172.
Debré, R. (1939). Quoted by Gates (1952).
Dible, J. H., Hunt, W. E., Pugh, V. W., Steingold, L., and Wood, J. H. F. (1954). *J. Path. Bact.*, **67**, 195.
Doig, R. K. (1957). *Med. J. Aust.*, **2**, 617.
—— and Pitman, F. (1957). Ibid., **2**, 612.
Gates, R. R. (1952). *Human Genetics*. Macmillan, New York.
Gebbing, M. (1936). *Dtsch. Arch. klin. Med.*, **178**, 472.
Hanhart, E. (1953). Quoted by Gates (1952).
Harvald, B., and Hauge, M. (1956). *Dan. med. Bull.*, **3**, 150.
Kallmann, F. J. and Reisner, D. (1943). *J. Hered.*, **34**, 269.
Karlish, A. J., and Tárnoky, A. L. (1960). *Lancet*, **2**, 514.
Lawrence, J. S. (1955). *Brit. med. J.*, **2**, 1616.
Marshall, A. G. (1953). *Brit. J. Surg.*, **41**, 38.
—— (1956). *J. Path. Bact.*, **71**, 95.
Moncrieff, A. (1953). *Brit. med. J.*, **1**, 1.
Newman, H. H. (1917). *The Biology of Twins*. Chicago. Quoted by Gates (1952).
Oswald, N. C. (1958). *Recent Trends in Chronic Bronchitis*. London.
Parsons, F. B (1939). Quoted by Gates (1952).
Race, R. R., and Sanger, R. (1954). *Blood Groups in Man*. Blackwell, Oxford.
Reid, D. D. (1958). *Lancet*, **1**, 1237.
Reid, L. (1958). In N. C. Oswald's *Recent Trends in Chronic Bronchitis*, p. 26.
Siemens, H. (1942). *Die Zwillingspathologie*. Springer, Berlin.
Singh, A., Jolly, S. S., and Kumar, L. R. (1961). *Lancet*, **1**, 587.
Sorsby, A. (1953). *Clinical Genetics*. Butterworth, London.
Stanbury, J. B. (1960). *Proc. roy. Soc. Med.*, **53**, 904.
Waterhouse, J. A. H. (1950). *Brit. J. soc. Med.*, **4**, 197.
—— (1953). In A. Sorsby's *Clinical Genetics*, p. 35.
Woodworth, R. S. (1941). *Heredity and Environment*. New York.

"We are studying Irish males, who are between the ages of 30 and 60 years, have lived in the Boston area for 10 or more years, and who have a brother in Ireland who has never left the country. Preliminary results on about 200 Irishmen in Boston and 60 blood brothers in Ireland indicate that those who remain in Ireland consume an average of 300 calories more per day, and yet weigh less. This obviously means more physical activity—walking and bicycling in Ireland. Those who remain in Ireland consume more animal fats, with 94% of the total fat intake coming from animal fats including an average consumption of a pound of butter per week, and yet they have lower levels of serum cholesterol than their brothers in Boston—a mean value over the total age range of 206 mg./100 ml. versus 222 mg./100 ml. Hypertension is less than half as prevalent among the brothers as compared with brothers in Boston."—Stare, F. J., *J. Amer. med. Ass.*, 1961, **178**, 924.

TREATMENT OF ANXIETY STATES BY ANTIDEPRESSANT DRUGS

BY

WILLIAM SARGANT, M.B., F.R.C.P., D.P.M.

AND

PETER DALLY, M.B., M.R.C.P., D.P.M.

From the Department of Psychological Medicine, St. Thomas's Hospital, London

For nearly four years we have been experimenting with the use of the new antidepressant drugs in a variety of psychiatric conditions. As a result of an early trial of iproniazid with a selected group of depressed patients, who had been referred primarily for electric shock treatment, one of us (Dally, 1958) reported that iproniazid was useful in mild depressive states, but that sometimes it increased symptoms of chronic tension and anxiety in this particular group of depressions. Further experience with this drug and its more recently developed analogues, such as phenelzine, isocarboxazid, and the like, used on a much wider range of patients, led us to modify this view, and we then isolated and described a group of what we called "atypical" depressions—cases which seemed particularly responsive to the monoamine-oxidase inhibitors (M.A.O.I.) (West and Dally, 1959; Sargant, 1960, 1961). This group included cases showing both hysterical and phobic anxiety symptoms, and sometimes the illness more closely resembled an anxiety hysteria or a reactive depression than a true endogenous depression. Since then we have come increasingly to recognize that these atypical depressions do overlap with, and are sometimes indistinguishable from, illnesses which many clinicans would very often label as anxiety neuroses.

Pure anxiety states are rarely seen in clinical practice because secondary symptoms of hysteria, depression, or obsessional thinking generally complicate the picture, especially when the illness has persisted for any length of time. Anxiety states have also generally been much more difficult to treat in a simple and satisfactory manner than have true depressions. It therefore seems of great importance from a therapeutic point of view to find now that M.A.O.I. used alone, or combined with chlordiazepoxide hydrochloride ("librium"), can often be very effective in the treatment of certain anxiety states, even where there may be no obvious sign of depression. Though the literature has in the past contained isolated references to the value of M.A.O.I. in states of anxiety and tension (Dickel *et al.*, 1959; Gallinek, 1959), yet with the intensive work and advertising of these drugs for the depressive states their value in the former group of patients has mostly been overlooked by psychiatrists and general physicians alike.

To illustrate these points we report the effect of M.A.O.I. drugs on 60 out-patients with neuroses, who had previously been diagnosed and treated as "atypical" or reactive depressions, anxiety hysterias, or anxiety neuroses. Such diagnoses, as we have suggested, often overlap each other. Fortunately, these patients were mostly well known to us, and had been attending the department for considerable periods of time. All the patients were first given a combination of M.A.O.I. and chlordiazepoxide. Subsequently the effect of giving each drug alone was tried. It was most important to find