MAY, 1954

THE ULSTER MEDICAL JOURNAL

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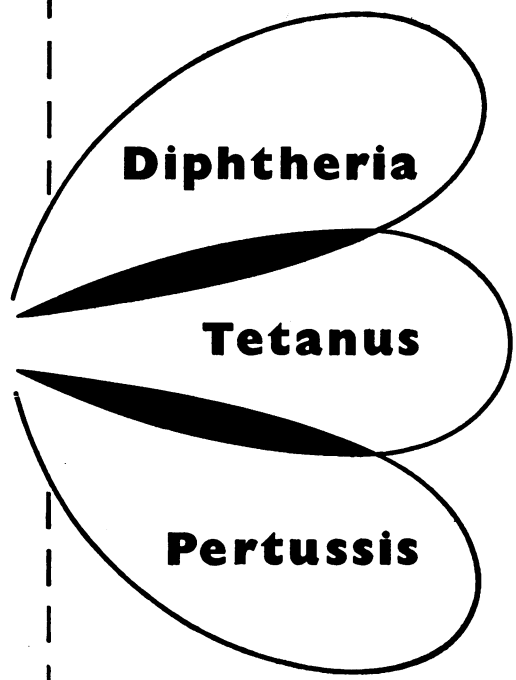

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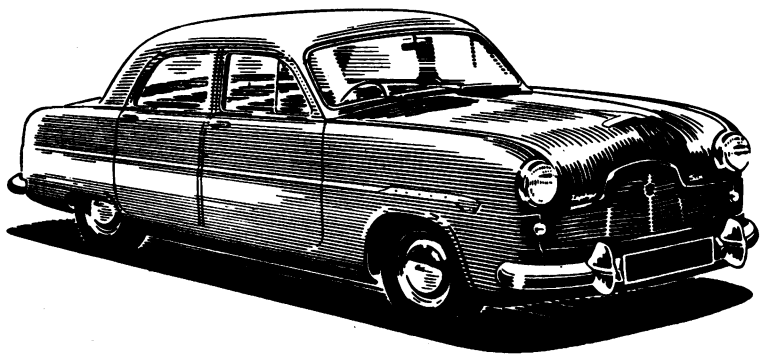

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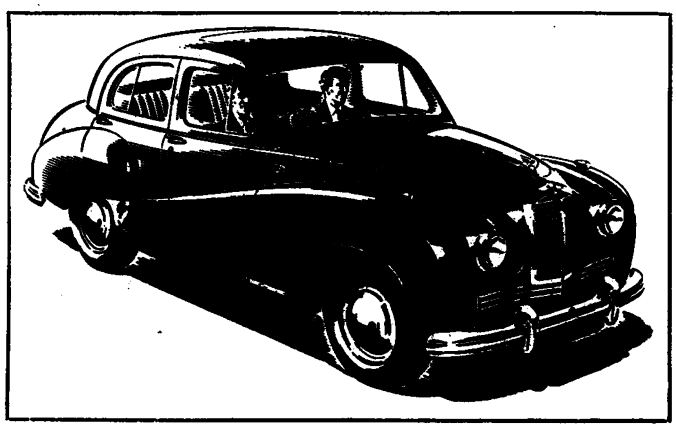

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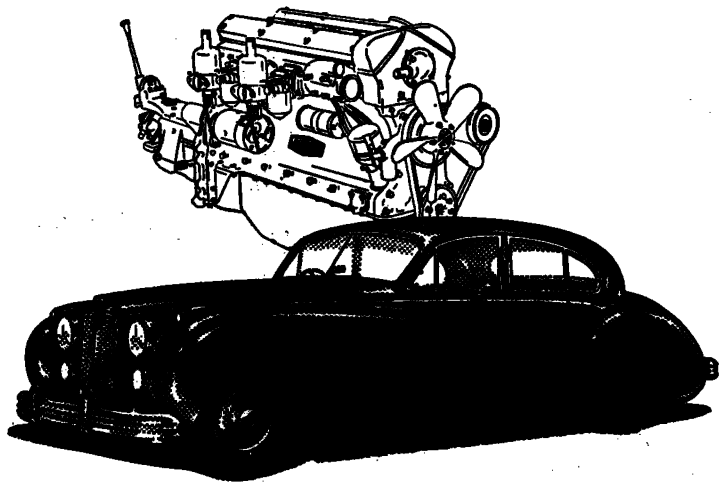

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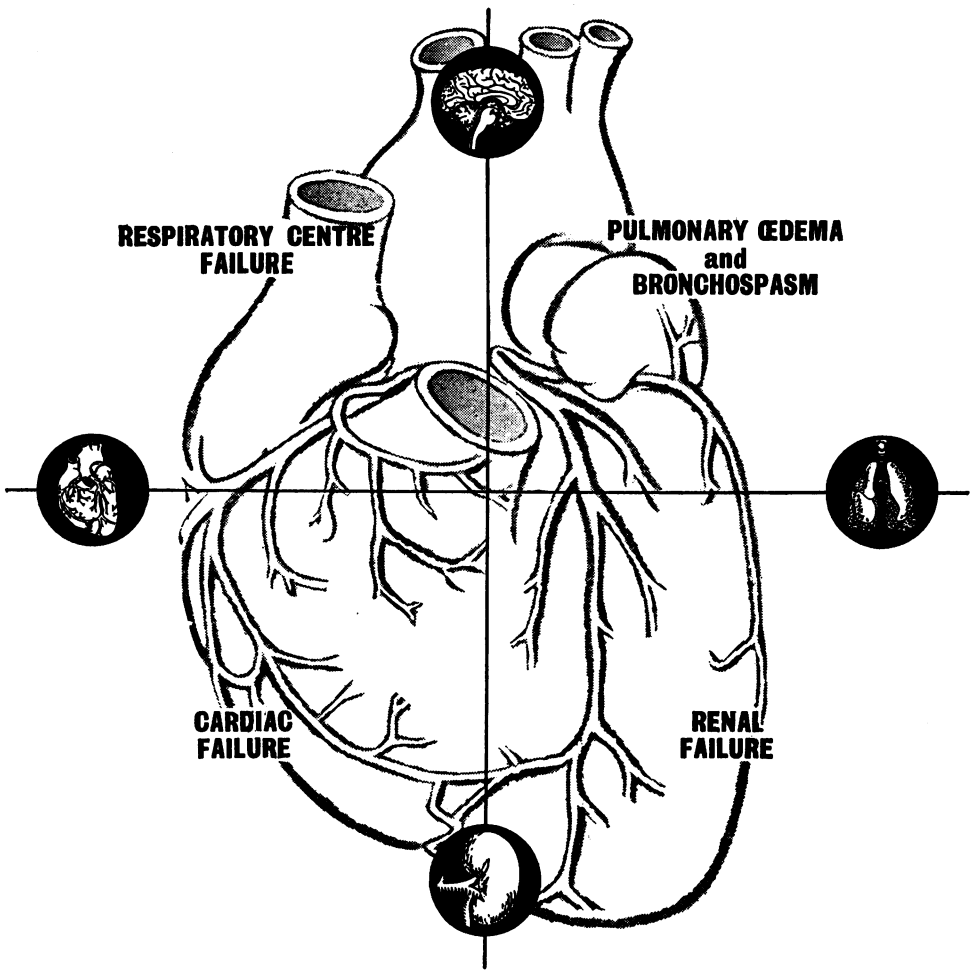

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(N:N'dibenzylethylenediamine dipenicillin G)

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Ph. 417

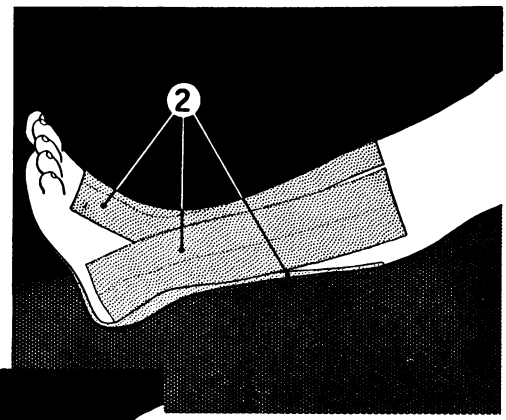
Elastoplast Bandaging Technique

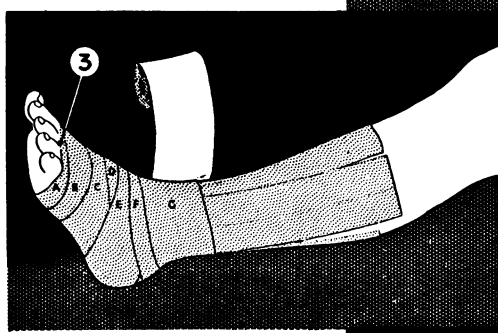
IN THE TREATMENT OF

Varicose Conditions

1 The leg should be elevated and the foot kept at a right angle to the leg.

2 If the limb is œdematous, or thin or the skin *devitalized*, vertical strips of Elastoplast should be applied before bandaging.





*3 Commencing at the webs of the toes, take two or three turns around the foot, dependent upon its length, and bandage around ankle enclosing heel as illustrated.

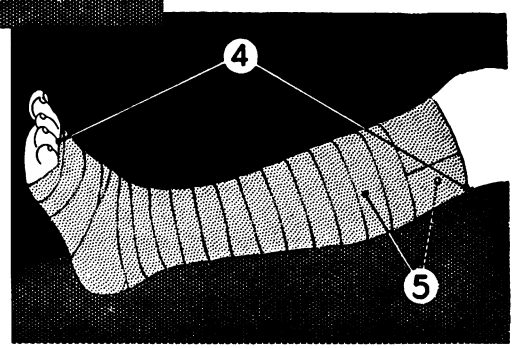
4 Leg should be *covered* from webs of toes to a point just below the bend of the knee.

5 Turns should overlap by at least half the width of the bandage (the yellow line down the centre of an Elastoplast bandage is a guide).

6 No creases.

7 Firm and even pressure proportionate to the amount of induration and œdema present.

* *Note bandaging may be made from toes upwards or knee downwards as desired.*



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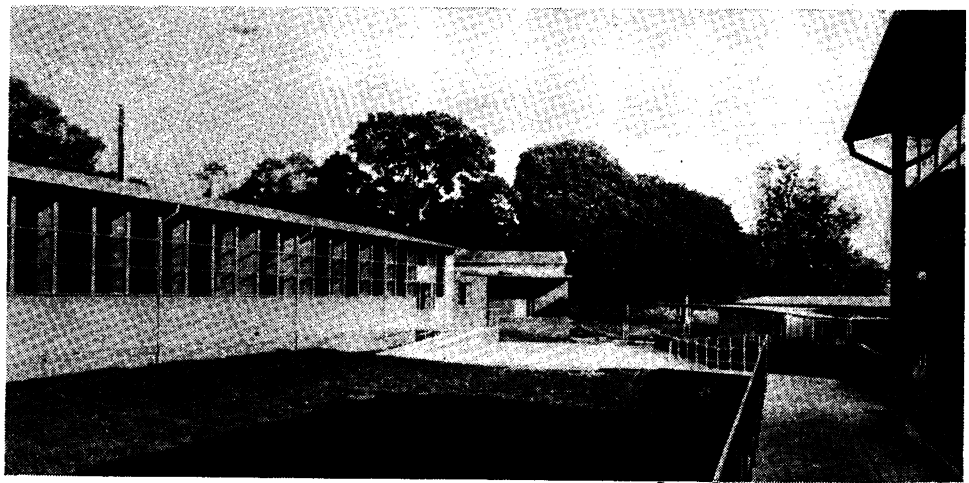

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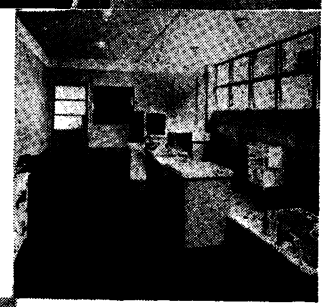

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THE ULSTER MEDICAL JOURNAL

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2. Manuscripts should be typewritten with double spacing and with wide margins. They should be fully corrected, and contributors will be responsible for the payment of any sum charged for alteration in printer's proof in excess of ten shillings per sheet (16 pages).
3. References should be given as in the publications of the British Medical Association and in most other modern British journals. If contributors are uncertain of the correct abbreviation for the title of any journal, as given in the World List of Scientific Periodicals, they should give the full title.
4. Tables and illustrations should be reduced to a minimum, and should be sent detached from the typescript of the paper. Line drawings should be used whenever possible. All illustrations must be in a finished form ready for reproduction. Half-tone blocks require to be printed on special art paper and are costly. Authors may be charged for these at cost price.
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It is hoped to issue two numbers each year: in May and in November.

THE ULSTER MEDICAL SOCIETY

THE MEDICAL INSTITUTE,

COLLEGE SQUARE NORTH, BELFAST.

Dear Sir (or Madam),

If you are not a member of the Ulster Medical Society, we would appeal to you to give the question of joining your consideration. The Society has been in existence since 1862, and has always been active in keeping its members interested in the advances in medical science as well as in current professional affairs. The Medical Institute, situated in College Square North, belongs to the Society (through the generosity of Sir William Whitla), and is ideally adapted for meetings, committee meetings, and recreation. There is a library with current medical periodicals, and facilities for reference to medical literature are available in conjunction with the library at the Queen's University. There is also a billiards-room available to members, and lighter periodicals are also provided. Meetings are held at intervals of a fortnight during the winter months, and papers are contributed by members. Distinguished visitors are occasionally asked to contribute papers on subjects upon which they are specially qualified to speak. **The Ulster Medical Journal, the official organ of the Society, is issued to all Fellows and Members free of charge.**

May we, therefore, appeal to you to join the Ulster Medical Society, and so enable us to widen its influence and sphere of usefulness still further? A proposal form is appended: your proposer and seconder must be Fellows of the Society.

If you do not wish to become a member of the Society, will you consider entering your name as a subscriber to THE ULSTER MEDICAL JOURNAL? The subscription is fifteen shillings per annum, payable in advance to the Honorary Treasurer.

We remain,

Yours faithfully,

W. G. FRACKELTON, *President.*
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.....19.....

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Postal Address.....

Year of Qualification and Degrees.....

.....

Signature of Proposer.....

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THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

Vol. XXIII 1st MAY, 1954 No. 1

A Long-term Follow-up of Gastro-Duodenal Surgery

By P. T. CRYMBLE, M.B., F.R.C.S.
Emeritus Professor of Surgery, Queen's University, Belfast

A Lecture Delivered to the Ulster Medical Society, 10th December, 1953

An attempt to contact stomach cases subjected to operation during the last thirty years so as to investigate the ætiology of the various conditions and to determine the benefits obtained and the penalties demanded by the different methods of surgical procedure.

"We are constantly misled by the ease with which our minds fall into the ruts of one or two experiences."—OSLER.

MATERIAL.

A long-term follow-up of 353 cases of gastric or duodenal conditions treated by surgical operation, 278 (76%) of which were traced.

Operation.	Number.	Group 1.	Group 2.	Group 3.	Group 4.
Gastro-enterostomy	139	75	33	16	15
Gastrectomy	69	22	27	9	11
Closure of perforation	18	12	5	1	0
Perf. closure and G.E.	17	7	4	1	5
Pyloroplasty	17	7	7	3	0
Wedge or cautery and G.E.	10	3	3	2	2
Adhesions	4	3	1	0	0
Ligature of left gastric	1	1	0	0	0
No reconstruction	3	2	0	0	1
TOTAL	278	132	80	32	34

Definition of Groups.

1. No stomach signs or symptoms since operation and no complications which might be attributal to the operation. For example, pulmonary tuberculosis, coronary thrombosis, arthritis or early death.

2. Show a slight infringement of one of the above rules.
   For example—return of pain abolished by giving up smoking; a slight attack of melæna due to dietary indiscretion (wedding cake and wine).

3. "If anything, much the same."

4. Definitely bad. Such as early death, or further operation.

Some Causes of Death.

Of the 278 traced cases 96 are dead, and here are some of the causes of death :—

Old age (70 or over)	17
Cancer	20
Cardiac	9
Pulmonary tuberculosis	7
Cerebral hæmorrhage	4

In 46 cases the operation was gastro-enterostomy and in 28 the operation was gastrectomy.

Delayed Appearance of Complications.

In 33 cases the appearance of complications was delayed 10 years or more.

Case.	Delay Period in Years.	Complication.
12. Gastrectomy	18	Pain.
34. G.E.	15	Pain.
39. G.E.	13	Death from perforation.
46. Closure of perf.	12	Heartburn and vomiting.
59. Pyloroplasty	16	Indigestion and waterbrash.
66. Gastrectomy	13	Angina.
69. Closure of perf. and G.E.	12	Cardiac death at 49.
72. G.E.	17	Cardiac death at 69.
77. G.E.	15	Melæna due to wedding party.
82. G.E.	18	Cardiac.
87. Closure of perf.	13	Arthritis.
93. G.E.	15	Melæna.
94. Gastrectomy	14	Arthritis.
97. G.E.	15	Death from cancer.
101. G.E.	19	Perforation and death from melæna.
121. G.E.	20	Death from pyloric cancer.
125. G.E.	10	Pulmonary tuberculosis—Death in 1 year.
135. G.E.	11	Cardiac death at 65.
147. G.E.	10	Melæna.

Case.	Delay Period in Years.	Complication.
150. Gastrectomy - - -	12	Death from coronary thrombosis.
157. Gastrectomy - - -	15	Anæmia.
159. Pyloroplasty - - -	21	Death from cancer of stomach.
161. Wedge resection and G.E. -	13	Death from pneumonia at 53.
163. Gastrectomy - - -	20	Death from cancer of throat.
164. Gastrectomy - - -	15	Death from chest trouble following gastric cancer.
171. Gastrectomy - - -	14	Nausea and vomiting.
182. Gastrectomy - - -	22	Pulmonary tuberculosis.
199. G.E. - - - - -	16	Cardiac.
221. G.E. - - - - -	18	Pain and heartburn.
223. Gastrectomy - - -	18	Leukæmia and death at 53.
235. Gastrectomy - - -	14	Wind in stomach.
237. Gastrectomy - - -	23	Angina.
246. Gastrectomy - - -	12	Stroke.

Ætiology.

Heredity.

Suggested in 12 cases.

Example—The father, who had married a cousin, died aged 81, had a bad stomach all his life and finally developed angina pectoris. Two daughters perforated and later required gastro-enterostomy and one son had a gastric operation.

Example—A family of six boys, five of whom had stomach operations.

Example (Case 188)—This case required gastrectomy for a large gastric ulcer. Her father, brother, and three sisters had stomach trouble.

Occupation.

Cases exposed to fumes or dust of some kind—petrol, whiskey, bleaching, French polisher, sewage - - - -	13
Thirty-one other cases occurred in :—	
House painters - - - - - - -	7
Joiners - - - - - - - -	8
Tram or busmen - - - - - - -	8
Barmen - - - - - - - -	4
Policemen - - - - - - - -	4

Anatomy.

Cases of gastric ulcer associated with a narrow pylorus - -	16

Other Causes.

Pulmonary tuberculosis - - - - - -	11
War experience - - - - - - -	6
Psychic influence - - - - - - -	6
Smoking - - - - - - - -	5
Drink - - - - - - - -	6

Possible Sequelæ.

Pain, hæmorrhage or vomiting.

Gastro-enterostomy	22
Gastrectomy	6
Closure of perforation	4
Closure of perf. and G.E.	1
Pyloroplasty	4
Wedge resection and G.E.	2

Span of life diminished.

Gastro-enterostomy	5
Gastrectomy	12
Closure of perf.	0
Closure of perf. and G.E.	3
Pyloroplasty	0

Cardiac.

Gastro-enterostomy	7
Gastrectomy	8
Closure of perf. and G.E.	1

Arthritis.

Gastro-enterostomy	2
Gastrectomy	3
Closure of perf.	1

Marked diet restriction.

Gastrectomy	6
Pyloroplasty	1

Pulmonary tuberculosis.

Gastro-enterostomy	5
Gastrectomy	2
Closure of perf. and G.E.	1

Nausea.

Gastrectomy	3
Pyloroplasty	1

Cancer.

Gastro-enterostomy	6
Gastrectomy	5
Pyloroplasty	1
Wedge resection and G.E.	1

Perforation.

Gastro-enterostomy	4
Gastrectomy	1

Anæmia.

Gastrectomy	8
Pyloroplasty	1

Jejunal ulcer and fistula.

Gastro-enterostomy	4

Stroke.

Gastro-enterostomy	1
Gastrectomy	2
Pyloroplasty	1

List of Those who have Passed the Age of 64

65 to 69.

Gastro-enterostomy	9 living	...	3 dead
Gastrectomy	8 living	...	5 dead
Wedge resection and G.E.	—	...	2 dead
Pyloroplasty	2 living	...	—
Closure of perf.	1 living	...	—

70 to 74.

Gastro-enterostomy	6 living	...	6 dead
Gastrectomy	7 living	...	1 dead
Closure of perf. and G.E.	1 living	...	—
Pyloroplasty	—	...	1 dead

75 to 79.

Gastro-enterostomy - - - -	2 living	...	2 dead
Gastrectomy - - - - -	1 living	...	2 dead
Pyloroplasty - - - - -	—	...	1 dead
Closure of perf. and G.E. - - -	1 living	...	—
Adhesions - - - - -	—	...	1 dead

80 and upwards.

Gastro-enterostomy - - - -	2 living	...	4 dead
Gastrectomy - - - - -	1 living	...	1 dead
Closure of perf. and G.E. - - -	1 living	...	—

LONG-TERM CANCER SURVIVALS.

Case 36.—Two-third gastrectomy on a woman of 52 in 1931. Still alive and well in 1953.

Case 100.—Two-third gastrectomy for pyloric carcinoma in 1936 on a woman aged 58. She was still alive in October, 1952, and may still be alive.

Case 164.—Sub-total gastrectomy for columnar carcinoma on a man aged 42 in 1928. He had no stomach trouble afterwards and worked as a driller in the shipyard. He died in 1943 of chest trouble (? lungs). He survived 15 years.

The material for this communication was obtained mainly from the Records Department of the Royal Victoria Hospital, Belfast, and from private notes made at the time of operation. It consists of cases which survived operation and were operated upon by me or a colleague as far back as 1923. The first step in tracing the cases is to write and ask the patient to come to the hospital for an interview. This was successful in about one-third of the cases and required the assistance of a part-time secretary-typist. I wore out two secretary-typists over the years, and I am much indebted to Miss Sayers and Miss McCann for their assistance. At the same time I should mention Miss Lutton, who is to be congratulated on the way she built up the Records Department, and I should like to suggest that we erect a bust or a plaque in her memory.

Now what about the remaining two-thirds? We have no department in the Royal Victoria Hospital which will undertake this work, and there is no text-book to give you any assistance. Here are some hints :—

1. Put your name down with the "Belfast News-Letter" for a copy of next year's Belfast and Northern Ireland Directory. You will be unable to buy a second-hand one.
2. Visit the address of the patient even if there is a new tenant. This is easy with the aid of the directory, but beware of slight errors in the case records. 6 Pim Street should have been 6 Pim's Avenue. McMurray should have been Murray. By the way, who fills in these details on the case sheet? Is it the sister, the staff nurse or the probationer? It must be quite a problem to obtain accurate information from a seriously ill patient. I should advise you to conduct the search by car, but leave the car in the main road and enter the

small streets on foot. The car will be safer in a main thoroughfare. Having arrived at the proper address, several things can happen.

(a) The patient is living in the house but has neglected to reply to the hospital letter. It is now quite easy to make contact.

(b) The new occupant of the house can give you the address of your patient or can give you the details of the death.

(c) You are directed to the oldest inhabitant in the street, usually a woman, and she can give you a clue. Some of the people have risen in the social world, but they move outwards along the same radius. Given the proper address, the country work can be done by letter, but even if there is a new tenant, a clue may be obtained.

Here was a difficult case—a young woman had married after the operation, left her occupation, changed her name and changed her address. Application to the original business produced the name of a relative in Lambeg—a sister—who directed us to a friend in Derriaghy who gave the final address as Stoneyford.

In the country we rely on the local shop, the police barracks or the post office: all of these are very helpful.

As a rule, the reception is quite friendly once they realise what it is all about. In 1953 I visited in a small back street off the Dublin Road with reference to a joiner (69 in 1924) who had a gastro-enterostomy. A sad-looking woman came to the door and admitted that this was where my patient had lived. I asked, "Are you his daughter?" "No, I am the grand-daughter, and what do you want?" "I am making some enquiries about him." "Are you not a bit late making your enquiries, as he died in 1931?" Some patients at first deny that they have ever had an operation.

Ætiology.

Having successfully traced a living patient many years after an operation, there is enthusiasm and interest in discussing the question of history. Histories before operation are usually recorded by resident pupils and obtained from an individual who is more concerned with a severe abdominal pain or with the anxiety of the outcome of a serious operation. If the whole operating business is over and done with, and patient and examiner have all the time in the world, full justice can be done to ætiology. As this would appear to be the most important part of gastro-duodenal disease, one had hopes that some clues might be forthcoming. Certainly we can record some facts, but whether a statistician would agree with our conclusions is another matter.

Hereditary.—In 248 traced cases only 12 suggested hereditary influence, but in these cases it was quite marked. Take, for example, a family of six boys, five of whom had stomach trouble, and another family of a father, two daughters and two sons, all of whom had stomach trouble (the two girls perforated and one boy had a gastro-enterostomy), the father had married his cousin, had stomach trouble all his life, successfully escaped operation (relative's statement), lived to be over 80, and died of angina pectoris. What is the weakness that is inherited? Is it

some anatomical peculiarity or some secretory defect or psycho-somatic weakness or gross neglect in the household of all the ordinary rules of diet controlling selection and preparation of food, the time of meals and suitable surrounding amenities. Being an anatomist of sorts, I am inclined to look for some naked-eye deformity, and I have noted that in 16 of the traced cases the pylorus was abnormally narrow. In 10 of these there was merely a narrow pylorus which could be treated by pyloroplasty, and in five the narrow pylorus was accompanied by one or more lesser curve ulcers requiring a gastrectomy. The sixteenth case was a muscular thickening of the pyloric canal and was dealt with by a gastro-enterostomy.

Occupation.—Some patients trace their indigestion to occupation, and in certain cases surgical experience would suggest that the occupation might be a factor. At the head of the list come the workers subjected to irritating or unpleasant fumes, e.g., petrol, whiskey, bleaching, aluminium, ropeworks, sewage disposal, tobacco dust, and, in one case, looking after a horse suffering from Decline of the Bowel. These include 16 cases in all. In other groups there were 6 painters, 8 joiners, 5 tram or busmen, 4 barmen, 4 dustmen, and 3 policemen.

Pulmonary tuberculosis.—Surgeons are well aware of the danger of doing a gastric operation on one with pulmonary tuberculosis and avoid these cases where possible. The difficulty is that a case may present with an obstructing duodenal ulcer and pulmonary tuberculosis. The physician is handicapped by the defective digestive system and a successful gastro-enterostomy may solve the problem, but the risk of early death is considerable. Another interesting point arises in this connection, and that is the appearance of pulmonary tuberculosis 5, 10, 15 or 20 years after a gastric operation. Is this to be claimed as a penalty or merely as an unconnected incident?

Pulmonary tuberculosis was a feature in ten of the cases, and six of these died within a few years of the operation (2 months, 2, 5, 7, 7 and 11 years). Four are living and well 15 to 24 years after operation.

Cardio-vascular.—It is not uncommon to find the gastric cripple dying of some cardio-vascular condition such as coronary thrombosis, a stroke or hardening of the arteries, but it has been suggested recently (Elkeles. *B.M.J.*, Nov. 21, 1953) that atheroma of the arteries may be a cause of gastric ulcer in elderly people. The abdominal aorta was radiographed in 732 cases over 50 years of age. Calcified lesions were found in 75 per cent. of 116 cases of chronic gastric ulcer and in only 4.3 per cent. of 70 cases of stomach cancer. One hundred and ninety duodenals showed 34.2 per cent. and 356 healthy controls showed 32.3 per cent. The conclusions drawn are, first, that gastric ulcer in people over 50 is due to insufficient blood supply and, second, that the presence or absence of calcified aortic lesions may be a valuable aid in differentiating between simple and malignant conditions.

Other Factors : Ætiology.—There are a number of strains, indiscretions or disasters which alone or in combination may be blamed for the onset of gastric or duodenal lesions. These include smoking, alcoholism, unsuitable diet, exertion,

war experience, financial trouble and domestic worries. A doctor gave me a wonderful history of his duodenal ulcer which produced severe hæmatemesis and finally obstruction. He was a chemist who worked under great strain to become a doctor. Irregular meals, cigarettes or sweets to stave off hunger, bad teeth, the mental strain of examinations, and finally doing his first locum by means of a bicycle—followed by a hæmatemesis.

One of my patients began work as an apprentice baker and blames his first dyspepsia on hot soda farls, fresh from the oven, made into a sandwich with brown sugar. Another patient and his relatives are quite satisfied that the care of a very smelly horse suffering from decline of the bowel was the start of his ulcer.

Penalties of Gastric Operations.

Sir Heneage Ogilvie, *B.M.J.*, August 9, 1952: "The only safe course is to advise gastrectomy in all gastric ulcers that are not rapidly and permanently healed by rest and diet. We can do this without hesitation because we know that the patient *will live happily ever afterwards.*"

Recent broadcast on duodenal ulcer—Physician: "The patient must learn to live with his ulcer and keep it in subjection. If he is not prepared to do this, he must *pay the penalty of an operation.*" Surgeon: "*There is no penalty* and *no restrictions* after operation. Ninety per cent. are cures and can lead an ordinary life."

You have the list before you of the possible sequelæ in my cases, and it is a formidable one. Many of these faults appeared ten to twenty-two years after operation and would not have been included in a short-term follow-up, and whilst some are without doubt connected with the original disease, such as pain, vomiting, hæmorrhage, cancer, nausea, marked limitation of diet, and perforation, others, such as arthritis, cardiovascular conditions and pulmonary tuberculosis are debateable.

Only 22 of the 69 gastrectomies can be placed in Group I, and the remaining 47 produced 57 of the possible sequelæ, some cases accounting for one or more conditions. Sixty-four of the 116 gastro-enterostomies attained Group I standard and the remaining 52 accounted for 56 sequelæ. The delayed appearance table shows the danger of relying on a five- or ten-year follow-up.

The Gastric Cripple.

Anyone who has undergone a stomach operation requires to exercise more discretion in habits than the normal individual if he or she is to avoid one or more of the sequelæ already described. Here are a few cases illustrating this statement.

Case 117.—A policeman, aged 26 in 1932, admitted as an acute abdomen. At operation a duodenal perforation was closed and a long appendix, full of fæces, removed. Hunger pain persisted for eight years, and his weight had diminished from 10 stone to 9 stone. He then gave up smoking, which meant 200 cigarettes and a quarter of an ounce of pipe tobacco a week. Following this courageous act, his weight gradually increased and is now 16 stone, and his indigestion is limited to evening duty (one month in four).

Case 156.—39 in 1936. A boilerman.

Gastric perforation in February, 1936, treated by closure.

March, 1937, three-fourth gastrectomy for hour-glass and great curve ulcer.

In 1946 he gave up tobacco (25 cigarettes a day and 3 ounces of pipe tobacco a week) as his indigestion was returning. Since then all symptoms have disappeared.

Case 230.—28 in 1941. A breadserver.

In 1929 appendix removed and an ideal kink freed (Mr. Kirk).

1940 : Gastro-enterostomy for stricture of the first part of the duodenum (P.T.C.).

1949 : Jejunal perforation closed (S. Irwin).

1950 : Vagotomy (Prof. Rodgers).

It is reported that he consumes a bottle of rum a day and smokes 20 cigarettes a day.

Case 161.—40 in 1928, and had done no work since the 1914-1918 war. Was reported to be a heavy drinker.

1928 : Wedge resection and gastro-enterostomy for small lesser curve ulcer.

1941 : Died of pneumonia following an air raid. He was in the Royal Hospital for lumbago and was taken down into an air-raid shelter.

Case 108.—A married woman, aged 37 in 1935, with a family history of stomach trouble.

1935 : Perforation in the region of the pylorus closed. Much soiling of the lower abdomen.

1936 : Became pregnant and subsequently had two pyrexial attacks. In May, 1937, died three weeks after a Cæsarean section. Death due to peritonitis.

Case 42—Police sergeant. 40 in 1927.

March, 1927 : Gastro-enterostomy for relief of pyloric obstruction.

May, 1927 : Died of pulmonary tuberculosis.

Perforation.

I regret that the numbers of perforation are so small in the communication, but it so happened that when I was a registrar the perforations were all done by the assistant surgeons and when, after some years I became an assistant surgeon, my senior called upon the registrar to do the perforations. Finally, as a full surgeon, I was expected to permit my tutor to close the perforations, and right well he did it, as he only had twenty of them and they all survived the closure operation.

Fifty years ago the mortality attending this operation was around 50 per cent., and it has been stated that the great Continental surgeon, Mikulicz, had 35 deaths in 36 cases. Well, we were doing better surgery in Belfast at that time as Surgeon Kirk, one of the pioneers of Ulster surgery, published a series of ten consecutive cases without a death. Furthermore, he was the first man to remove a gall bladder in this school. Prior to this, the Ulster surgeons had been content to remove gallstones.

Vassalloo (*B.M.J.*, May 2, 1953) reports a series of 673 closures with only one death, a most remarkable achievement.

In this communication we can report on 17 cases of simple closure of perforation, and the follow-up result is excellent.

Group 1 - - -	11	Group 3 - - -	1
Group 2 - - -	5	Group 4 - - -	0

Closure of the perforation, plus gastro-enterostomy, was used in the other 17 cases with results that are not so impressive.

Group 1 - - - 7		Group 3 - - - 1	
Group 2 - - - 4		Group 4 - - - 5	

Pyloroplasty.

Twenty-three cases, 14 of which have been traced. The operation mortality was nil, and the grouping of the traced cases was :—

Group 1 - - - 5		Group 3 - - - 3	
Group 2 - - - 6		Group 4 - - - 0	

This operation should be considered where the patient complains of attacks of pain and vomiting, the X-ray shows some gastric retention, and on opening the abdomen the surgeon finds a non-cicatricial narrowing of the pylorus and no other pathological condition. This finding was noted at all ages from 20 to 66 years of age.

It is a safe operation with few penalties and some excellent results.

Case 47.—A girl, aged 20 in 1927. Vomiting attacks in childhood; recently pain 15 minutes after food; one attack of melæna; weight had decreased from 7 stone 11 lb. to 5 stone 11 lb. X-ray showed retention.

Operation—pyloric canal in state of spasm for 20 minutes and was hard and white. Finally, the spasm passed off. Pyloroplasty performed.

Follow-up in 1953. Twenty-six years after operation. Now weighs 13 stone. No stomach symptoms since the operation. Is under treatment for diabetes mellitus, but leads an active normal life.

Three of the 14 traced cases are now dead. One at 79 of a stroke, one at 70 of a stroke, and a third at the age of 47 of cancer of the stomach. Two of the remaining cases were operated upon by other surgeons and gastro-enterostomy performed. The list consists of 9 females and 5 males.

Gastro-enterostomy.

When I entered the field of surgery 45 years ago the technique of the operation was stabilised—a posterior retrocolic gastro-enterostomy with a 2½-inch vertical stoma, in the same sagittal plane as the incisura angularis and avoiding the great curvature vessels. The afferent limb of the jejunum joined the stomach near the lesser curve, and the efferent limb of the jejunum descended vertically from the great curvature.

The problem to-day is not *how* to do the operation but *when* to do it. Being interested in radiography, most of my cases were selected for operation by the presence of seven-hour gastric retention. Having opened such an abdomen, a gastro-duodenal search might reveal a pathological condition, but if this were negative then one examined for adhesions, gallstones, kinked appendix or colon stricture. One of the most marked cases of visible peristalsis of the stomach was produced by a simple stricture of the ascending colon.

All my surgical life I have been doing gastro-enterostomies and obtaining, I thought, quite satisfactory results. Recently so many attacks have been made on this operation that I began to wonder : "Am I living in fools' paradise?" Hence

one of the reasons for this investigation. Well, the figures show that gastro-enterostomy in my hands is still the most satisfactory gastric operation.

Sixty-four (57 per cent.) out of 116 traced cases attain Group 1.

Twenty-two (18 per cent.) out of 116 traced cases attain Group 2. Why has this swing from gastro-enterostomy to gastrectomy developed?

Possible reasons are :—

1. Selection of unsuitable cases for gastro-enterostomy.
   Avoid (*a*) Pulmonary tuberculosis.
   (*b*) Young males with a non-obstructing duodenal ulcer.
   (*c*) Heavy drinkers.
2. The bad result is widely known whilst the good results are never seen again. Example—Case 149. Twenty-three in 1931. Gastro-enterostomy for a non-obstructing duodenal ulcer. Stomach trouble off and on ever since, but continued working for twenty years. In the past two years has been in hospital nine times for examination.
3. Great claims for gastrectomy which still require proof.

GASTRECTOMY.

Out of a total of 85 cases who survived operation, 69 have been traced (81 per cent.), and 16 are still untraced. The grouping result is :—

Group 1 - - -	22	Group 3 - - -	9
Group 2 - - -	27	Group 4 - - -	11
Total - - - - - - -		69	

Thirty-two of the cases are still alive, and 37 are dead.

The operation was usually performed for cases of medium or large ulcers, and very occasionally for carcinoma.

The most prominent complications or penalties were :—

	CASES		CASES
Span of life diminished -	12	Cancer - - -	5
Cardiac - - -	6	Nausea - - -	3
Anæmia - - -	8	Arthritis - - -	3
Marked diet restriction -	6	Pain or vomiting - -	3

In forty-nine of the traced cases the result might be said to be satisfactory and the patients admitted great improvement in spite of the fact that a number of them were experiencing the penalties which may be demanded. Apart from adopting medical treatment for the small gastric ulcer or pyloroplasty for the small gastric ulcer combined with a narrow pylorus, gastrectomy would appear to be the correct procedure in the case of a medium or large gastric ulcer. At the same time some quite good long-term results have been obtained in the treatment of a high hour glass by anastomosing the two pouches and draining the lower pouch by a gastro-enterostomy.

A comparison of the long-term results between gastro-enterostomy and gastrectomy where the gastro-enterostomy was performed for the relief of duodenal ulcer and the gastrectomy for the relief of gastric ulcer.

All the cases were operated upon in the period 1923 to 1931 and by the same surgeon. The technique of the gastro-enterostomy has already been described in this paper whilst the gastrectomy was Bilroth 2 type—removal of one-half or two-thirds or three-quarters of the stomach, and retrocolic end to side gastro-jejunostomy with a three-inch stoma. In four of the cases an antecolic operation was used owing to absence or shortness of the transverse mescolon, and in these cases the efferent limb of the jejunum was attached to the lesser curve of the stomach. In one case the pyloric canal was left in situ, but in the others the pylorus was included in the part of the stomach removed.

LONG-TERM FOLLOW-UP TABLE.

	Gastro-enterostomy	v.	*Gastrectomy*
Traced	70 (83.3%)	...	34 (85 %)
Untraced	14 (16.6%)	...	6 (15 %)
Average age	38	...	41
Dead	29 (41.4%)	...	24 (70 %)
Dead over 70	10 (14.2%)	...	5 (14.7%)
Alive	41 (58.5%)	...	10 (29.4%)
Group I	36 (51 %)	...	8 (23 %)
Group II	17 (24 %)	...	18 (53 %)
Group III	13 (18 %)	...	4 (11 %)
Group IV	4 (5.7%)	...	4 (11 %)

CONCLUSIONS.

Follow-up.—The period selected for investigation was 1923-1948 and included 353 cases, of which 278 (76%) were traced. Since this paper was presented on December 10, 1953, before the Ulster Medical Society, twenty-nine additional cases have been traced. Of these, eighteen are alive, eleven are dead, fourteen were graded Group I, fourteen were graded Group II, and one Group IV. One would hope therefore, that amongst the 24% of untraced cases quite a number are still alive and well. The investigation is still proceeding, and letters sent out some years ago are still producing responses. One patient had emigrated to Philadelphia and only received his letter when he returned to Strabane on a holiday and two years after the letter had been delivered locally. He had his operation in 1930 (gastro-enterostomy for duodenal ulcer) and reports the present condition as "100% successful."

Such cases as "domestic servant in Joy Street," sailor from a foreign ship, inmate of a lodging-house, a name like John Smith, and the woman who marries after operation prove exceedingly difficult.

Operations.

The chronic dyspeptic might be placed in one of five classes.

(*a*) Medical treatment only.

(*b*) Some extra-gastric operation required, such as adhesions, gall bladder, appendix or colon stricture.

(*c*) Pyloroplasty for congenital narrowing of the pylorus or after excision of a small duodenal ulcer.

(*d*) Gastro-enterostomy for duodenal ulcer, avoiding the young male, the case of pulmonary tuberculosis, and the chronic alcoholic. Most suitable for duodenal obstruction in the middle-aged and elderly.

(*e*) Removal of half or two-thirds or three-fourths of the stomach for medium-sized or large ulcers and for carcinoma.

I have no personal experience of gastrectomy for duodenal ulcer, but I would draw your attention to the long-term follow-up table, where there is a comparison between gastro-enterostomy (for duodenal ulcer) and gastrectomy (for gastric ulcer). These are all the cases done in the period 1923-1931 by one surgeon, and gastro-enterostomy gives much better results in the category Group I and in those alive. Six of the gastro-enterostomies lived beyond the age of 80 and two of these are still alive, one aged 82 (plays bowls and can do a double knee bend) and the other 87 (a retired blacksmith). I have encountered five jejuno-colic fiistulæ and one jejunal perforation. Two of the fistulæ did quite well by separating the two bowel limbs and closing the two apertures, but the other two fistulæ both died following a more extensive operation. The jejunal perforation is still alive, following simple closure.

The delayed appearance of complications and sequelæ which appeared ten to twenty-two years after the operation has been disclosed by the research. Such cases in a short-term follow-up would have been graded as Group I results. They include gastric symptoms, pulmonary tuberculosis, cardio-vascular lesions, and cancer. Cancer appeared at varying times after operation in twelve cases, and the situations were—stomach five times, colon five times, and œsophagus twice.

A Criticism of the Present-Day Management of the Barren Woman

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"And when Rachel saw that she bare Jacob no children, Rachel envied her sister; and said unto Jacob, Give me children, or else I die." (Gen. 30: 1.)

MAY I remind you of the old love story of Jacob, Leah and Rachel, the daughters of Laban. Jacob first married Leah and she bore him a succession of sons. Later he married her sister Rachel, and though it was Rachel that he really loved, she remained barren. Indeed, it is here that we read of the earliest treatment for barrenness. Rachel begged Leah for mandrakes, but was spitefully refused. And how much nicer is the English word 'barren' than the modern usage of 'sterile' or 'infertile.' However, to be scientific, one must use classical words, even though they do not express one's meaning so exactly as the words of our mother tongue. To me 'barren' means 'having failed to bear,' whereas both sterile and infertile signify 'unable to bear.' But I hope you will find me an unscientific man—I shall quote you no figures—I shall show you no tables or percentages.

I want us to consider the present-day management of the barren woman and to assess critically all the devices and procedures that we use for her benefit.

When I first studied gynæcology, all that was ever done was to dilate the cervix uteri, and many women conceived thereafter. Then came Rubin's test or insufflation, and we could now pronounce a woman barren with some certainty—it rather shook our complacency when women conceived after we had proved their tubes to be sealed, but now we have excuses for that. Then came salpingography and more certain demonstration of where and to what degree tubes were sealed. With the elucidation of male and female hormones a bright day dawned, for now we could control ovulation and spermatogenesis, we could make imperfectly developed uteruses come to maturity and we could grow decidua where none had been before—or so we thought. Then came the discovery of what a large part genital tuberculosis played in infertility in women. Finally, with the realisation that the male partner was often at fault, came the scientific investigation of the semen—its quantity, its quality, and the ability of the sperms to penetrate cervical mucus. Testicular biopsy may reveal the extent and the causation of male infertility. So we have advanced a long way from the haphazard fiddling with the cervix uteri that we did twenty-five years ago—*or have we?*

Infertility clinics were established. Now what is a clinic? A clinic is a cheap way of getting a medical problem dealt with. It is suddenly realised that certain

groups of clinical conditions are common and crowd the Out-Patient Department to the exclusion of more interesting pathological material—vaginal discharges suffered the same fate. These cases are therefore got rid of by making a special clinic for them, and a junior is put in charge. He is an aspiring young man or woman and he wants to impress that this is good work he is doing. He reads all the work of the research workers and proceeds to apply it to the patients attending. After a while he has some "statistics," and he publishes an article to show what good, thorough, and up-to-date work he does. His rivals go one better and do even more at their clinics, and publish articles that hint that it is almost criminal to fail to carry out as many and as drastic tests as they do. The seniors catch the infection and, for fear of seeming old-fashioned, they take to practising the new regime.

Amid it all, what of the patient? She has come not to find out how barren she is, nor why she is barren nor to have treatment for some condition which she did not know was present. She has come because she wants to conceive. If the routine of many clinics is followed, she could not possibly conceive for the next six to twelve months. If she is curetted one month she is insufflated the next or her husband is urged to repeated masturbation or even to submit to the removal of a portion of a testicle. I want to put to you quite seriously the idea that all special clinics should be stopped and that a man seeing out-patients should, ideally, be prepared to carry out all the examinations and treatments he would do in private practice. In the time available to me, may I comment on some of the methods adopted?

Cervical Dilatation.

It *does* appear that all sorts of different interferences with the cervix render a woman more likely to become pregnant. Almost all the procedures that we do in treating barrenness involve some degree of manipulation and trauma of the cervix. Insufflation and salpingography involve trauma to the cervix. The old-fashioned empirical dilatation of the cervix was often followed by conception and so are the tests mentioned. Most of us have met the case when simple bimanual examination has been quickly followed by conception. The woman who has been hoping for a child for four or five years at last plucks up courage to ask for treatment. She is examined to exclude gross pathology and her name put on a waiting-list to attend for further investigation. When she is sent for, she is found to be pregnant. Consider another observation. Why is it that, in the absence of contraception, there is an average delay of six months before a newly-married couple conceives? Can we fit these observations together? May it not be that Nature demands an actively working and secreting cervical mucosa before conception is favoured? In the virgin the vault of the vagina is sterile and for most of the time the cervical canal contains an almost solid plug of gelatine-like mucus. In the married nulliparous woman the cervix is larger, the cervical glands more active, and the cervical mucus is more freely secreted and more fluid. The vault of the vagina is often not sterile. Did Nature intend that the mild trauma and mild infection of coitus should awaken the cervix to its more active state? This would account for

the observations I have quoted. Coitus may have failed to awaken the cervix mechanically or by mild infection. Our rougher handling of it by simple examination, by dilating it or by thrusting instruments into it may be effective. Perhaps this is all that happens when someone puts a retroverted uterus into another position.

Rubin's Test or Insufflation.

Gas is blown through the Fallopian tubes and the effect is not only diagnostic of whether they are patent, but it is said to have therapeutic value in that the tubes are cleared of any obstruction present. A typical graph shows an initial rise to overcome the resistance either of mucus or of spasm in the tube, then a fall as the gas passes through, and then it settles down with more or less regular slight rise and fall indicating the peristalsis in the tubes or, as some hold, in the uterine cornua. By listening with a stethoscope one can hear the gas coming through one or other tube. If there are peritubal adhesions the peristaltic waves are lacking and the gas goes through at an even, high pressure. Do you believe it all? The graph of a uterus removed by hysterectomy shows the same oscillations that are attributed to peristalsis. On the other hand, it is a common observation that a hystero-salpingogram will often show tubes to be patent when they had appeared to be sealed on a kymograph tracing.

If the gas goes through at all it proves that the tubes are patent, and I do not think any other conclusions can be drawn. It is my belief that the typical normal curve is what one would expect of gas bubbling through a fluid—a slightly sticky fluid. The gas would come through in little bursts and so cause the ups and downs. It is claimed that tubal insufflation has a therapeutic value in that it separates adhesions of the tubal mucosa and so creates a canal where there was none before. I have read an account where only on the ninth attempt did the surgeon succeed in forcing the gas through, and he claimed that he had opened a previously sealed tube. When we consider the fine, careful technique necessary at operation to perform salpingostomy and how, in spite of it, we so often fail to leave the woman with a patent tube, I cannot believe that blowing a tube up until it bursts its adhesions can possibly produce a functioning canal where none was before. No, the only value of tubal insufflation is to be able to say to the woman, "You may have a child." It cannot be used to say to the woman, "You cannot have a child." Any other benefit derived from the procedure is, in my opinion, due to the dilatation of the cervix and not to the retrograde passage of gas along the tube.

Salpingography.

It has often been remarked that when insufflation has failed the injection of lipiodol is more likely to succeed in persuading a woman to conceive. It has been claimed that the oil can force its way where gas could not or that it has an antiseptic value and clears the tubes of mild infection. I cannot agree that, by forcing its way, the injected substance would do any mechanical good, and I just do not believe that lipiodol (or the other contrast media) is so beautifully antiseptic that it clears an old-standing salpingitis in one application. I would attribute the better results from lipiodol injection to the fact that greater injury is done to the

cervix. Insufflation is done with a cannula 3mm. in diameter. For salpingography a volsella is necessary or a wide cannula is screwed into the cervix. In fact, one is back to the old-fashioned cervical dilatation.

Hormones.

I think I can say that I know of no hormone available to me that will make a woman ovulate naturally. Œstrogenic hormones, if anything, inhibit ovulation. Progesterone will convert proliferating endometrium into secretory, but what is the good of doing that if the woman has not ovulated and produced her own progesterone? The two hormones together will mimic normal menstruation, but no matter how they are used they will not make a Graafian follicle ripen, rupture, and produce an ovum. Chorionic gonadotrophin has been used for sterility in homœopathic doses—doses that will do no harm and may have a psychological effect, but, quite frankly, I know of no hormone treatment of infertility that is not just a mixture of hope and suggestion. Perhaps both hope and suggestion have their value.

Tuberculosis.

It has been shown that tuberculous endometritis may be quite symptomless except for sterility, and it has also been shown that these cases always have tubal tuberculosis. The tubercles in the endometrium may be so scanty that we are enjoined always to curette out the entire endometrium, and I have read of cases where the diagnosis was only established after eight full curettings. If one receives a surprise report from the pathologist that there are tubercles in the endometrium, the case will not be accepted for publication as a true diagnosis unless tubercle bacilli are seen or animal inoculation proves positive, so that a further curetting may be necessary to produce material to inject into a guinea-pig. When the diagnosis has been made the patient is to have up to 1 mgm. per day of streptomycin up to a total of not less than 100 mgm. This will take four months. A curetting is done at two months to see how the process is improving and, on the completion of treatment, a further curetting is done to make sure that it has been effective.

I want to put to you that we have no idea of the natural history of endometrial tuberculosis. If these women were left alone would they come to any harm? Consider tuberculosis anywhere else in the body. Given good general health and complete and utter rest, the process becomes quiescent. The last thing one does is to irritate it mechanically or to give the faintest chance for secondary simple infection to gain access. If we do these things we are courting active tissue destruction and the spread of tuberculosis. And here we are scraping, scraping, scraping inside a tuberculous organ. We don't know what would become of the patient if we left her alone. If you tell me that you have watched a woman with tuberculous endometritis go on to the production of symptoms and signs, may it not be that the manipulations and infection necessary to make the diagnosis set off activity in the disease? What became of these patients before we realised that silent tuberculous endometritis was possible? Every now and then we opened an

abdomen and found an old shut-off fibrous or caseous lesion or a hydrosalpinx, but it was not often and certainly not in the numbers that are now diagnosed in sterility clinics. The rest settled down and the woman lived a healthy, untroubled life.

The next point is that one would expect streptomycin or isoniazid to deal effectively with the endometrial lesions—they are primary, miliary foci, well supplied with blood, for they are discarded every month and fresh ones appear; but one would not expect antibiotics to deal with the tubal lesions which are usually older caseous lesions. Hence the common finding that, after a full course of treatment, the endometrial tubercles recur. If you say that many do not recur, I would remind you that you have done something more than give streptomycin. You have allowed many months to elapse and tuberculosis tends to cure itself with the passage of time. Sharman (1952) states :—"In those patients who were followed up, the lesion remained active, but did not appear to be progressive nor cause much general disturbance to health. They remain sterile, however, and may suffer from minor menstrual abnormalities." I would not deny streptomycin to these patients and indeed I always give it, but I would strongly deprecate the repeated curetting that has been advocated, and I would rely much more on maintaining good health with peace and quiet to the pelvis for a long time.

Basal Temperature Records.

By this means we could tell whether a woman was ovulating and when she was ovulating. Her basal temperature is recorded very carefully over a period of months—that is, her body temperature on first waking in the morning and before rising. The thermometer is usually placed in the vagina for ten minutes. At ovulation there is a typical diphasic peak—a rise, a fall and a rise again higher than before—like a square root sign. If this does not occur she has not ovulated.

Now I can assert without fear of contradiction that no woman has ever conceived as a result of intercourse with a thermometer. Whether she ovulates or not in any given menstrual epoch does not foretell what she will do at the next. If she does not ovulate, is there anything that one can do to make her ovulate? I think not. To know that she ovulates at a certain fixed time may allow us to advise her to concentrate on that time, but who is to know at the next ovulation whether she will stick slavishly to her previous routine. In Hamlet's words :—

". . . and yet, within a month—
Let me not think on't—Frailty, thy name is woman."

There is a firm which publishes a special chart for women to record their basal temperature and their menstruation over many months. I say that to ask a woman to carry out this useless procedure month after month is morbid, conducive to introspection, and destructive of the freedom and abandon that is essential for the success of this natural function. Is she to conceive by the calendar, to copulate by the clock?

Let me quote from Siegler and Siegler (1951) :—

"This test is fallible in a certain number of cases and the monophasic temperature

graph typical of the anovulatory cycle may sometimes be found associated with a secretory endometrium and even with conception."

Investigation of the Male Partner.

Simple clinical examination of the male may show some congenital or acquired abnormality that is a complete bar to fertility, but this is not enough. The semen must be examined by taking a masturbation specimen—indeed, it is now established that repeated seminal analyses must be performed, and I have seen it written that one should not pronounce on a seminal specimen until at least eight samples have been examined. In pursuing this line of enquiry a dreadful ogre has come into being—a seminologist. Around this so-called speciality the usual fantastic façade has been built. So, soon as one seminologist writes that he always examines four specimens before issuing a report, his opposite number writes that six are necessary and the next man bids eight, dropping dark hints that many seminologists are not up to their job. The colour, liquefaction, number, character, and density of the sperms are to be noted. Straightway at every infertility clinic all the men are urged to repeated masturbation.

And what does it all amount to? The only qualification a seminologist needs is that he can recognise a normal spermatozoon when he sees one and that he can count. If there are normal sperms present in any numbers it is possible for the woman to become pregnant. The normal count is 80,000,000 per cc. I have known a woman to conceive when her husband's count was 40,000 only. Their chance is less, but the couple has not come to be told that conception is impossible, or unlikely, or that they have only 12.3% chance compared with others. They have come to be helped to have a child if this is possible. If it is not possible, we must be very, very careful not to add to their distress. Now I know of *no* treatment of *any* value in *any* form of male infertility. Epididymo-vasostomy for stricture of the vas is about on a par with transplantation of the ovary into the uterine wall—the opportunities for doing it are rare, and when it is done the chance of success is very, very small. Swyer (1953) gave testosterone implants to 56 sub-fertile men. Twenty-eight improved and 28 were unaffected or got worse. It is easy to say it was worth it for the 28 who improved. But this is hopelessly unscientific. What we must also know is how many would have improved if none had had implants—perhaps even 56!

Testicular biopsy may show the pathology behind a man's infertility, but does it do anything to help the pair to have a child? When the cause is found, can anything be done about it? A great deal of what is published is research work—new work discovering new facts about the factors inimical to conception. It is necessary that this work should be done, because only thereby can we learn anything about the subject and hence learn to treat it. But it is quite unnecessary that this research should be repeated in every infertility clinic throughout the country. Unless you have some new line of enquiry you should not subject all the male partners to repeated examination to prove that they are infertile or relatively so—they have come to see if you can help them. As you cannot help sub-fertile men, leave them alone and tell them that pregnancy is possible.

Psychological Effects.

Finally, I want to consider the psychological effects not so much of barrenness as of our management of it. We recently received a letter from the Principal Medical Officer of one of her Majesty's prisons asking for details of our contacts with an inmate who was in considerable psychological difficulties. His wife had come to us on account of her barrenness and all tests showed her to be normal. The husband was then examined and a seminal specimen showed only a few spermatozoa, some of them motile. A kindly conscientious doctor told him that it was unlikely, though not impossible, that he should become a father. I was interested in this and asked the prison medical officer if I might have details of the man's record. He had always been somewhat of an inadequate personality, but had never been in serious trouble before. Soon after being told of his sexual deficiency he had indecently assaulted two little girls and landed in gaol. "He was over-attached to his mother and jealous of his father, who begot eleven children by his mother; he feels that he will never prove himself fully virile (and his father's equal) if he cannot beget even one child. The result appears to have been a regression to childish modes of feeling and action with the concomitant urge towards childish sexual partners. The associations have not yet been fully worked out, but this is the general interpretation; he was carried back to his childhood difficulties and acted out his frustration in a childish way."

Here is a man, certainly of poor mental fibre, but a man who had never been in serious trouble before. He is told by a very conscientious and kindly doctor that it is unlikely that he can fertilise his wife. He thereupon commits a horrible offence, and we say it is his fault for being so subnormal, anyway—it isn't—it is our fault. Was there any need to tell him of something which we cannot put right and which could only harm his self-esteem and his wife's esteem? Exactly the same applies to the wife when she is found to be at fault. Does it do any good to tell her that conception is impossible or unlikely? If we can do something to help her—yes; but if we cannot—no. I think we should look on both of them as a pair, and it should not be part of our duty to apportion blame at all. So far as possible, I think we should keep secret what we have found unless it is something we can put right. How does Nature let a woman know that she is barren? Slowly over the years it comes to her that she is not conceiving. Though she may never arrive, she travels hopefully. Slowly she develops other interests—she sublimates her maternal instincts into other channels. I grant you that she may have some heartaches in that time, but they do less harm than the brutal statement that pregnancy is impossible or that her husband cannot fertilise her. In matters of this kind, the male is the weaker vessel, and is apt to react very badly when informed that he is sterile. The female probably suffers more, but is less apt to show it by drastic and dramatic action.

Recent Developments.

My thoughts had travelled so far and I had put them down on paper when the October (1953) number of the "Journal of Obstetrics and Gynæcology of the British Empire" came. It contained two items of great interest. First is an article

written by my friend, Linton Snaith, and his colleagues, one of whom was a statistician. Some of his conclusions were :—

"There was no difference in pregnancy rates between those who had received some form of treatment, and those who had not, even after making allowance for differences in duration of infertility between these groups.

"Data from the 1 per cent. sample of the 1951 census are considered so as to get estimates of the probability of conception after a given duration of marriage, and these estimates closely correspond with those obtained from the study of those women who attended an infertility clinic, whether or not they received treatment.

"The value of the infertility clinic for therapeutic purposes appears to be slight."

The second item of interest in the Journal was an advertisement—it reads :—

"The American Society for the Study of Sterility announces the opening of the 1954 contest for the most outstanding contribution to the subject of infertility and sterility. The winner will receive a cash award of one thousand dollars, and the essay will appear on the programme of the 1954 meeting of the Society. Essays submitted in this competition must be received not later than 1st March, 1954. For full particulars concerning requirements of this competition, address The American Society for the Study of Sterility, c/o Dr. Herbert H. Thomas, Secretary, 920 South 19th Street, Birmingham, Alabama.

"The author should append on a separate sheet of paper a short biographical sketch of himself and include a photograph to be used in the necessary publicity should he be the winner of the award."

Gentlemen, that thousand dollars is mine. But, seriously, I wonder how many marriages will be broken, how many healthy people will be dis-eased, indeed, how many women will lose their lives in the course of this contest.

Suggested Management of the Barren Couple.

Destructive criticism is not very clever, and so far I have given you nothing but destructive criticism. What then *is* worth doing when a woman comes complaining of her barrenness? We have reorganised our hospital management of the condition, and I thought you would like to hear what we do now. The patient is first seen in the ordinary out-patient consultations, and whilst I am opposed to special clinics for specific conditions there is no doubt a matter like this can only be dealt with effectively with some degree of privacy. A patient complaining of her failure to conceive is seen, perhaps with students present, and is examined in the ordinary way to exclude major gynæcological abnormalities. She is then given an appointment and asked to attend *with her husband*. At this meeting they are interviewed together, and it is explained to them that some not very disturbing tests are to be carried out to make sure that there are no minor correctable abnormalities, but that we do *not* propose to end by laying blame on either of them, and that at the end of these investigations we shall see them together again and advise them what their prospects are. If the husband then offers himself for the simple clinical examination, he is examined to exclude abnormalities. The wife has

insufflation carried out as an out-patient, usually about five days after a period has ceased. If this is difficult in any way it is not persisted in, but she attends as an out-patient for insufflation under thiopentone. She is then given an appointment to attend in three months for a post-coital test. A fortnight before that test she is written to in case she is pregnant or her period has varied, so that a post-coital test would be useless. If live spermatozoa are found in the intra-cervical mucus nothing further is required of the husband. If none are found, he submits a specimen. We are then in possession of as much information as we need and are ready for the final interview. One can divide the cases into three categories :—

1. We have found nothing whatever wrong. These are told that there is every prospect of success and that, as they are both fully normal, it would be wrong to do anything further.

2. We have found some factors inimical to pregnancy. If these factors are treatable, such as cervical erosion, chronic cervicitis or a small fibroid, the couple is offered treatment. If they are not treatable, such as a low-sperm count in the man or a degree of uterine hypoplasia in the woman, they are still told that there is every prospect of success, but they are advised to return in six months for a second *and final* insufflation under an anæsthetic with dilatation of the cervix.

3. We have found something which appears a complete bar to conception, such as azoospermia in the man or tubal occlusion in the woman. These are told that pregnancy is possible but unlikely, but in the same breath we say that we do not propose to inform them which of them is at fault, for we can do nothing about it, for neither of them is really suffering from any disease. We do not raise the question of adoption with them, but if they raise it we approve and help them.

Now these are very rough grades and may require variation with each couple. For instance, not all couples are of equal levels of intelligence or emotional balance. We are quite capable of telling a couple in the third group that they are perfectly normal if either or both of them appears to be of the wrong temperament to accept the position.

Throughout it is essential to keep up an atmosphere of hope and encouragement. We must remember that when a couple comes to us complaining of their childlessness they are not complaining that they are ill—they are complaining merely of a dysfunction. To treat them as though they are ill or to make them ill by our treatment is a grave disservice.

> Rachel cried: "Give me children, or else I die." . . .
> And many years later: "God remembered Rachel, and God hearkened to her, and opened her womb. And she conceived and bare a son" (Gen. 30: 22, 23).

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Otosclerosis and a Review of Fifty-One Fenestration Operations

By KENNEDY HUNTER, M.B., F.R.C.S.(ED.)

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OTOSCLEROSIS is a disease of unknown ætiology. The microscopic pathology is a spongification of the bone of part of the otic capsule. The affected area is softer than normal bone and contains an excessive number of marrow spaces and thin walled blood vessels. The lesion is usually bilateral, circumscribed, and occurs in the site of predilection, i.e., in the region of the otic capsule between the cochlea and vestibule, just anterior to the foot plate of the stapes. From this area the lesion may extend and involve the basal turn of the cochlea and round window. Other areas are occasionally involved. The disease must cause ankylosis of the foot plate of the stapes in order to produce the characteristic clinical features.

Heredity plays an important part, and a family history of deafness is present in a certain proportion of cases. This is often stated to be in the region of 50 per cent., but in our series of cases there was a definite family history in only about 18 per cent. of cases. It is more common in females than males, the usual figure is about 85 per cent., but in this series it is about 70 per cent.

The deafness first makes its appearance between the ages of 15 and 30, the extremes in this series were 9 and 39 years. Pregnancy and severe illness may cause deterioration. Tinnitus is a usual symptom, and sometimes it is the presenting one. Sixty per cent. of this series made some complaint of tinnitus. Giddiness occasionally occurs, but only 4 per cent. of the present series mentioned this symptom. Paracusis Willisi is a characteristic finding, i.e., patient can hear better in the presence of a noise. In this series of fifty-one cases, only six had no paracusis, but its presence or absence was not recorded in six cases, i.e., thirty-nine gave a definite or doubtful answer.

The tympanic membrane and Eustachian tubes are normal unless altered by some other disease. The deafness is of a conduction or middle ear type, except in the very advanced cases, i.e., air conduction is reduced, but bone conduction is very little altered, i.e., Rinne's sign is negative.

The diagnosis is suggested when a young woman complains of increasing deafness, tinnitus, and paracusis, with normal tympanic membranes. Atypical cases, of course, occur when the lesion involves the inner ear. Here various combinations of conduction and perception deafness occur, and these are the cases which present difficulty in diagnosis.

There is no cure for the lesions of otosclerosis. Very many types of conservative treatment have been advocated, but none has proved of any benefit. Hearing aids

are of great value in improving the hearing of persons suffering from otosclerosis. They are of most value in the type of case considered to be ideal for operation.

Joseph Toynbee's description in the nineteenth century of otosclerosis and of ankylosis of the stapes led surgeons to investigate the possibility of operative measures to enable the sound waves to by-pass the middle ear obstruction and reach the intact cochlea. Kessel, in 1876, removed the stapes, but where this was possible, infection usually supervened. Later the promontory was trephined and the opening covered with a muco-periosteal flap. No lasting improvement was obtained, and often the hearing was made worse. Jenkins, of London, in 1913 was the first to make an opening in the external or lateral semi-circular canal, but improvement was only very short-lived. In 1917, Holmgren, of Sweden, made an opening in the superior semi-circular canal, which could be covered by dura, hoping to delay or prevent bony closure. Sourdille, of Nantes, made an opening in the lateral semi-circular canal, and covered the opening by a muco-cutaneous flap continuous with the tympanic membrane. His operation was done in two, three or more stages. In 1938 Lempert, of New York, described a one-stage operation with approach through the meatus. This is the basis of the modern fenestration operation.

Before operation each patient is given a printed note of explanation of what to expect after operation, and the correct post-operative behaviour.

The operation is performed under general anæsthesia. Perfect anæsthesia and a relatively bloodless field are essential for the success of the operation. An endaural incision exposes the cortex of the mastoid and bony meatus. The mastoid antrum is opened and the bridge and outer attic wall are removed. This exposes the incus, and the head and neck of malleus. The incus is removed and the head of malleus cut off at its neck. At this stage, the presence of ankylosis of the stapes is confirmed by direct vision and palpation with a fine probe. The meatal skin is carefully separated from the bony meatus and cut, so that it is hinged on the drum. It is then fitted over the exposed lateral semi-circular canal. If correct, it is turned back and protected with green protective.

The second stage of the operation is done with the aid of an operating microscope giving a magnification of six to ten. Continuous irrigation of the wound is arranged and the fenestra made in the lateral semi-circular canal opposite the stapes by means of dental burrs. Periosteal and endosteal bone is removed from the canal until a faint blue line appears. This is caused by the cavity of the canal shining through the thinned bone. Next a gutter is drilled round the blue line, and eventually the cap so marked out is lifted off, exposing the cavity of the bony canal with its membraneous canal partly filling the lumen. The lower part of the new opening or fenestra is about 1 mm. from the facial canal; great care is required to avoid injuring the facial nerve. The continuous irrigation keeps the bone from becoming hot and so damaging the nerve, in addition to carrying away the bone dust, which might cause the fenestra to close by new bone formation. The fenestra is about 5 mm. by $\frac{3}{4}$ mm. The flap is then replaced over the fenestra and covered with green protective. A skin graft may be used to cover the raw surface. The

cavity is packed with marine sponge in order to get even pressure on the flap. The skin incision is closed.

On recovering from the anæsthetic, the patient shows signs of irritation of the labyrinth; these are giddiness, vomiting, and nystagmus. This gradually subsides in 24-48 hours, but balance is disturbed for a longer period. The wound is not touched for six or seven days. The first dressing is done under Pentothal anæsthesia. The cavity is slow to heal, as it requires time for the epithelium to line the whole cavity; the shortest time is about six weeks, but it usually takes much longer. No complications have occurred in this series of cases.

The improvement in hearing is usually not noticed for a few weeks after operation, and it may not reach its zenith for two to three months. Bony closure of the fenestra may take place up to two years after operation, but it is unlikely to happen after one year; if it does take place, the hearing will return to its preoperative level. It is possible to reopen the canal, but the results are not good.

The ear with the worst hearing is usually chosen for operation, so that, in the event of it being unsuccessful, a hearing aid may still be worn in the unoperated ear.

The selection of cases suitable for operation is a difficult problem. The key is the state of the inner ear. There is no point in providing a passage for sound waves into the inner ear if it is not capable of transmitting the impulses to the brain. There is, as yet, no absolutely reliable test of inner ear function. Bone conduction is probably the best test.

Cawthorne stresses the importance of three other points in assessing the function of the inner ear :—Alteration of the timbre of the voice; an uncomplicated case of otosclerosis speaks with a soft, well-modulated voice; a loud speaking voice suggests inner ear involvement. Inability to hear really well with a hearing aid and disappearance of paracusis also suggest inner ear involvement.

An improvement of thirty decibels can be expected in a suitable case. A higher gain is sometimes obtained, but should not be anticipated. A patient with less than thirty decibels loss for the speech frequencies is not greatly handicapped. When the loss is more than thirty decibels, this brings the hearing loss above the thirty decibel line. This patient is very satisfied. Supposing one operates on a case with, say, seventy decibel loss for the speech frequencies. A successful operation result will again give an improvement of thirty decibels, but this still leaves the patient with a forty decibel loss. As this is below the thirty decibel line, the patient will still feel deaf. However, there are cases which may be able to use a hearing aid after operation where it was useless before operation.

The operation is not dangerous. In about 10 per cent. the hearing in the operated ear may be made worse by the operation and a very small percentage, about one-quarter per cent. the hearing may be lost in the operated ear. The ear with the worse hearing is operated on first. If this is successful, the other ear may be operated on after an interval of about two years.

Results.

An interval of eighteen months must elapse before assessing results. Some immediate successful cases may lose the hearing gained because of bony closure

of the fenestra. This usually occurs during the first year after operation and is unlikely after eighteen months.

Of our series of fifty-one cases, only thirty-one have been operated on eighteen months or more, so only these cases will be quoted.

USEFUL RESULT			RELATIVE OR COMPLETE FAILURE		
VERY GOOD	GOOD	MODERATE	SLIGHT	NO CHANGE	WORSE
35 Db. and over gain	25-34 Db. gain	15-24 Db. gain	5-14 Db. gain	0-5 Db. gain	
16%	33%	19%	16%	3%	13%
TOTAL, 68%			TOTAL, 32%		

It must be remembered that the deafness in this disease is progressive. Even if no actual improvement follows operation, the achievement of a stationary level of hearing represents some ultimate gain to the patient.

I would like to pay tribute to Dr. Jim Elliott, consultant anæsthetist, for his patience, skill, and help; also to the registrars in the department, especially Mr. R. S. McCrea, for their help in the after-treatment, and to the nursing staff for their very essential part in the treatment.

REVIEW

AN APPROACH TO GENERAL PRACTICE. By R. J. F. H. Pinsent, M.A., M.D.(Cantab.). (Pp. viii + 166. 12s.) Edinburgh: Livingstone, 1953.

HERE is an excellent book on general practice. It is written by a general practitioner, whose careful observation, recording, and analysis throughout years of general practice in an industrial area has produced this protocol of facts. All the difficulties of form-filling and certification which state medicine has produced are clearly stated and explained, much valuable advice and counsel is given in the every-day running of a general practice, and any doctor contemplating entering this branch of medicine would do well to study this book and gain by the experience of one who evidently loves his work and has made a success of it. W. J.

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Staphylococcal Pneumonia

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STAPHYLOCOCCAL pneumonia is a well-recognised complication of epidemic influenza. Chickering and Park (1919) described 155 cases, and more recently 66 cases were recorded by Finland, Peterson, and Strauss (1942). Smaller series have also been reported, and both the virus influenza A and the staphylococcus were isolated from patients by Scadding (1937) and Michael (1942). It can also occur as a primary pneumonia or as a complication of staphylococcal pyæmia.

This paper is based on fifteen cases of pneumonia, in whose sputa a coagulase-positive staphylococcus aureus was isolated in pure or almost pure culture. Only four of these occurred during an outbreak of influenza, Type A-prime, in Belfast in the months of January and February, 1951. The remaining eleven had, as far as we could ascertain, no connection with influenza. Primary staphylococcal pneumonia unassociated with influenza is usually reported as a disease of children. In them the mortality has been high. Kanof, *et al.* (1939), had a death rate of 65 per cent in twenty-three cases. Smaller series have been recorded with mortalities from 14 to 100 per cent. All our patients were adults, whose ages ranged from 21 to 74 years. The literature on cases which do not follow influenza is comparatively scanty. Reimann (1933) described six complicating various debilitating conditions. Yet post-mortem reports on pneumonia suggest it may be commoner than is usually thought. Gaspar (1941) found staphylococci in 38 out of 144 autopsies on pneumonia in seven years.

The prognosis in the various forms of staphylococcal pneumonia has shown considerable variation. The fulminating staphylococcal pneumonia following pandemic influenza carried an 82 per cent. mortality (Chickering and Park, 1919). Finland, Peterson, and Strauss (1942), using sulphonamides, had a mortality of 32 per cent. Brock (1945), in his thirty cases, had six deaths. Gibson and Belcher (1951) were able to describe ten cases associated with influenza treated with penicillin, all of which survived. In our series there was one death in hospital. This confirms the remarkable improvement in the prognosis following the introduction of antibiotics.

CRITERIA FOR DIAGNOSIS.

The standard of the M.R.C. for the diagnosis of specific bacterial pneumonia is to find "the pathogenic bacteria on mouse inoculation, blood culture, culture of

pleural fluid, or from the lung at autopsy; and in the case of staphylococcus aureus predominant only in the sputum, when this is clinically consistent and cultures from other sources are negative." Two main difficulties were found. It was not possible to do routine blood cultures or mouse inoculation tests. Secondly, many patients with suspected pneumonia are partially treated by their practitioner, and are only admitted to hospital when they do not show a prompt response, so that many sputa show no pathogens. We have made the diagnosis if the sputum, taken immediately after admission and before therapy, showed a predominant growth of a coagulase-positive staphylococcus aureus, or if this organism was found persistently in spite of therapy.

Clinical Features.

Before the introduction of penicillin, the course was as follows :—The onset was insidious, rarely with rigors or pleural pain. The fever was of the high remittent type, but the pulse was relatively slow. Labial herpes was rare. The patient appeared gravely ill from the first. Signs of lobar consolidation were uncommon. Scattered areas of impaired air entry and crepitations were more usual. These commonly involved both lungs. The sputum at first was small in amount and purulent. Sometimes it was pink in colour. Frank hæmoptysis was rare. Culture revealed the staphylococcus as the predominant organism.

X-ray usually showed at first areas of patchy consolidation scattered through a lobe of one lung or both lungs. These tended to become larger and coalesce. In the fulminating cases there was massive consolidation, usually of several lobes. Death often occurred at this stage. Sporadic cases before penicillin therapy usually developed cavitation. Cavities were frequently extremely large, with very thin walls, and in the cases which recovered they usually slowly disappeared, leaving no trace or minimal fibrosis. This supports the concept of their production by tension (Brock, 1945). They were liable to rupture, producing a pyopneumothorax, especially in children. Occasionally one or more thin-walled cavities persisted, giving a radiological picture like congenital cysts.

Because of antibiotics our cases have differed from the description given above in a number of ways. They fell into two groups—those who were and those who were not gravely ill.

Cases of Moderate Severity (Cases 1 to 11).

There were eleven such patients, all being males except one. Age did not appear to be of significance, the average being 36.5 years, with a range from 13-65 years. Usually the illness commenced with pleural pain, rigors, and cough, while increasing dyspnœa was a prominent feature in over one-third of the series. The sputum was yellow and thick, being often tinged with blood. Most cases were clinically indistinguishable from pneumococcal lobar pneumonia, and were admitted to hospital after the failure to respond to treatment for several days at home or within a short time of onset because they appeared very toxic. Two patients had a pleural effusion when admitted and one a collapse of the right lower lobe. Herpes febrilis only occurred in one case. No history of any definite precipitating factor

could be found in almost half of this group. Intercurrent disease was present in two cases, one had tabes dorsalis and the other mitral stenosis. Two patients had had recurrent chest infections within the previous few years—recurrent pneumonia and recurrent empyema respectively. The latter was found to have a healed collapse of a thoracic vertebra. The last two cases in the group may have harboured the staphylococcus in the mouth and nose; they gave histories of a tooth extraction two days before the onset and of a boil a fortnight previously.

Complications in these patients during their acute illness were varied. Four cases had effusions, including the two with this finding on admission. One effusion loculated in the oblique fissure could not be aspirated. The fluid obtained in two was cloudy and in one definite pus. The staphylococcus was cultured in two, while the remaining effusion which occurred in the second week was sterile. All cleared with antibiotic therapy. Only in two patients were there cavities, and these were only temporary. The remaining difficulties encountered were the onset of heart failure with auricular fibrillation, where the pneumonia complicated mitral stenosis, and the occurrence of staphylococcal abscess on the thigh after two days in another patient. This abscess was presumably septicæmic in nature and cleared rapidly after incision. With treatment, ten cases recovered extremely well; minimal fibrosis and pleural thickening being the only residue in three of them. The remaining patient developed three more attacks of pneumonia within five months and had a severe degree of fibrosis. Penicillin was the initial therapy, with one exception, and was adequate in six, but required to be replaced in four patients. Streptomycin produced recovery in three and aureomycin in one.

Response to treatment in these cases was satisfactory, and the course of the disease was very different from that described before the introduction of antibiotic therapy.

Illustrative Case Histories.

Case No. 3.—J. H., male, aged 40. Eight days before admission he developed a pain in the left side of his chest. He lost his appetite and energy. The day before he entered hospital this pain became much more severe, and was associated with severe dyspnœa and a cough. He had had an operation on his chest in childhood of which no details were available.

On admission, his temperature was 101.8 degrees. Grunting, painful breathing was present. The lower half of his left lung was dull. There was a pleural rub just above the left nipple. Breath and voice sounds were diminished. X-ray film showed a pleural effusion and the ninth right rib had been previously resected.

Penicillin and sulphamezathine were started on admission without response. Streptomycin was given instead of the latter drug, on the fourth day, and continued for five days, during which there was a clinical improvement. The fever reached normal in four days. Penicillin was then given alone for a further ten days.

Paracentesis of the chest produced a cloudy fluid, from which a pure growth of *Staph. aureus* was cultured. Sputum on admission and one week later showed a pure growth of the same organism, which was sensitive to penicillin, streptomycin, and to chloromycetin. After seventeen days' therapy only coliform organisms were grown. He had 6,400 leucocytes per c.mm., of which 68 per cent. were polymorphonuclears. Blood culture and lung puncture were sterile. Paracentesis was repeated in fourteen days and was straw-coloured and sterile.

There was a steady improvement in his general condition. Serial films showed a progressive clearing of the effusion. After two months there were only minimal signs of pleural thickening.

Summary.

Staphylococcal pneumonia with effusion in a previously healthy man, organisms grown from both sputum and fluid. Complete recovery with penicillin and streptomycin. Empyema did not develop. This case illustrates the value of antibiotic therapy.

Case No. 6.—H. McI., male, aged 65. Four days before admission he had a series of chills and pain below the right breast. Next day a productive cough commenced. The sputum was said to have been blood-stained. There was a history of two previous attacks of pneumonia four and three years ago respectively.

When seen, he had a temperature of 102 degrees. He was dyspnœic, but not cyanosed. There were signs of consolidation at the right base and a pleural rib in the axilla. The sputum was muco-purulent and, on culture, produced *Staph. aureus*. X-ray of the chest showed a patchy consolidation of the right lower lobe.

Penicillin was commenced. The temperature fell to normal on the fifth hospital day. There was a rapid improvement in his general condition. From the twelfth to the seventeenth day in the ward the temperature rose to 99-100 degrees daily. This coincided with the development of a small effusion which proved to be amber-coloured and cloudy. It contained a few lymphocytes and polymorphonuclear leucocytes. There was no growth on culture. This fluid disappeared in two weeks. The patient left hospital feeling fit.

He had three further attacks of right lower lobe pneumonia during the next five months. These were caused successively by a streptococcus pyogenes, a pneumococcus, and *Staph. aureus*. On each occasion there was a rapid response to antibiotic therapy. In the second attack of staphylococcal pneumonia the organism was penicillin resistant, but sensitive to aureomycin. Dental caries and chronic sinusitis were satisfactorily treated. Bronchoscopy was carried out twice and revealed no abnormality.

Serial chest films were taken during a period of six months. Finally, the patient was left with a considerable degree of fibrosis in the right lower lobe, with thickening of the pleura. Tomography showed a reticular pattern of residual fibrosis. It was considered that a lobectomy of the right lower lobe was indicated, but the patient refused permission.

Summary.

Staphylococcal pneumonia of the right lower lobe, complicated by a pleural effusion. The acute attack responded to penicillin. Resolution was incomplete and recurrent attacks of suppurative pneumonia followed. Extensive fibrosis occurred in the affected lobe.

SEVERE CASES ASSOCIATED WITH INFLUENZA (Cases 12 to 15).

There were four such cases. They all followed an influenza-like illness and occurred at a time when there was an epidemic of influenza (Type A-Prime) in the city. The influenza had occurred from one to three weeks before their admission to hospital. They had improved initially but their condition had subsequently deteriorated. All cases were gravely ill on admission. One case had only a low-grade fever, the temperature never rising above 99 degrees. This was a case of chronic bronchitis, emphysema, and pulmonary heart disease, who developed auricular flutter and heart failure during the pneumonia. Each of these cases showed an extreme degree of prostration, dehydration, and mental confusion. They all developed central cyanosis. Signs in the chest were those of a widespread bronchopneumonia. These signs changed from day to day. They were accompanied by radiological evidence of involvement of new areas of the lung. Large amounts of

thick purulent sputum were produced. This obstructed the bronchi and in three cases produced collapse of the major portion of one lung. On several occasions considerable improvement, which was life saving, followed removal of this tenacious sputum by mechanical suction from the bronchi. The response to penicillin was unsatisfactory and in all cases streptomycin was substituted. One case failed to recover on the latter but did so on aureomycin. There was residual fibrosis in all cases, and in two of them bronchography revealed bronchiectasis. One of the latter died at home five months later after several further attacks of pneumonia. A female in her sixty-fifth year died in hospital.

Illustrative Case Histories.

Case No. 14.—M. J. C., female, aged 38. For some years she had suffered from chronic bronchitis and had been under observation at a chest clinic. Two weeks before admission she developed influenza. Her recovery was incomplete and she was confined to bed by weakness. Three days before admission she experienced a severe pain in the left side, with an increase in her cough and sputum. The latter was described as "brownish."

On admission, she was emaciated and extremely cyanosed. There was well-marked dyspnœa at rest. Her temperature initially was 100.8 degrees. She was dull over the lower part of the left side of the chest, anteriorly and posteriorly. In the same area there were fine crepitations. At the left base there was an area of bronchial breathing and there was a pleural rub in the left axilla. There were also crepitations at the right base. The sputum was muco-purulent. Culture revealed a pure growth of *Staph. aureus*. She had 14,900 white blood cells, of which 86 per cent. were polymorphonuclear. X-ray of the chest showed that the whole hemithorax was opaque. The mediastinum was displaced to the left. It was considered that the left lung was collapsed.

Bronchoscopy was carried out and mechanical suction produced thick tenacious sputum. There was considerable improvement in the patient's general condition following this.

Penicillin was given on admission, but the staphylococcus proved to be resistant to this drug. A course of streptomycin was then given, with a good response.

Serial X-ray films showed considerable re-expansion of the left lung after suction through the bronchoscope. The signs did not completely resolve and fine crepitations were still audible at the left base on her discharge. It was obvious that resolution in the left lower lobe was incomplete. Pneumonectomy was considered to be indicated, but the patient refused her consent. This patient had three further attacks of pneumonia within a few months of leaving hospital. She died at home in the third of these.

Summary.

A case of acute staphylococcal pneumonia occurred in a chronic bronchitic subject. It was complicated by collapse of the left lung due to tenacious sputum. Mechanical suction was of great benefit in the acute phase. Drug resistance required streptomycin and, despite response to this, she was left with extensive lung fibrosis. Later she had two recurrences and in one developed a bronchopleural fistula. Pneumonectomy was declined by the patient, and she died from a third recurrence.

Case No. 15.—S. J. K., female, aged 64. There was a history of influenza, with fever and generalised pains in the body three weeks before admission. She made a poor recovery, developing dyspnœa, a copious yellow sputum and pain in the right chest on deep breathing. Treatment with a sulphonamide had no effect. Five days prior to admission her general condition began to deteriorate. She became confused mentally and had copious sweats.

On admission, she was extremely dyspnœic, with fifty respirations per minute. Her pulse rate was 124 per minute and her temperature 98 degrees. Moderate cyanosis was present.

Dullness was found at the right base and the entire right chest was filled with coarse rales. The trachea was deviated to this side. There were crepitations at the left base. The sputum produced a pure growth of *Staph. aureus* sensitive to both penicillin and streptomycin. X-ray examination was not possible owing to the weakness of the patient and her mental confusion.

Treatment with penicillin was commenced. After the first two days the temperature became elevated to 100-101 degrees, where it remained in spite of change of therapy to streptomycin. The sputum became more viscid and the general weakness of the patient prevented active expectoration as well as postural drainage. She died on the fifth day, having had three mega units of penicillin and 11 grm. of streptomycin.

Summary.

Post-influenzal atelectasis, involving most of the right lung, with superimposed infection by the *Staph. aureus*. Toxæmia was profound. Death appeared to be due to obstruction of the airways by thick viscid sputum. In retrospect, bronchial suction and the use of atomised hyalinuronidase and streptokinase would probably have been useful.

Discussion.

Staphylococcal pneumonia complicating influenza still remains an illness of great severity, and our small series all were gravely ill. Previous chronic bronchitis was of poor prognostic significance. The effects of obstruction of the bronchi by purulent sputum with subsequent anoxia, and collapse of a major portion of the lung, was a predominant feature. General weakness and toxæmia made the management of these patients extremely difficult. Mechanical suction, although dramatic in its effect, was a major procedure, with the inherent difficulty of passing an endotracheal tube blind in a conscious and distressed patient. Through this tube a bronchial catheter was passed attached to the suction pump, and it required frequent clearing owing to thickness of the sputum blocking the lumen. The final mortality, with only one patient alive after a year, was high. Survival of the acute illness with damaged fibrosed lungs was followed by bronchiectasis or by death after further pneumonic episodes, or death from the development of right heart failure with suppurative bronchitis.

In the series of patients who developed staphylococcal pneumonia without preceding influenza, the outlook was much brighter. Most made an eventual complete recovery, while the remaining quarter were left with some residual fibrosis. Recurrent pneumonia was only found in one case. Antibiotics would appear to have overcome the infection in these patients. Penicillin was usually sufficient, although streptomycin was required in some and aureomycin substituted in one case. The response to penicillin must be kept closely under review, and the onset of drug resistance anticipated if the response diminishes. With antibiotic therapy the differentiation of staphylococcal from other pneumonia was not usually possible on clinical grounds. Some treatment outside hospital had, in most cases, been given, and the main finding was that the response had been slower than anticipated. It was probable that the dosage of penicillin given in the conditions of domiciliary practice, while sufficient to overcome the usual more sensitive pneumococcus, was insufficient to cure, but did modify this type of infection. Patients treated for over a week before admission were found to be those requiring streptomycin or aureomycin, and an increase in penicillin resistance may have occurred. Antecedent

factors of significance were only found in half this group, and it is probable that many more cases of staphylococcal pneumonia occur than the literature would suggest. Purulent effusion was the commonest complication, but cleared with medical treatment. Cavity formation was only seen in two patients, and was of a temporary nature.

Summary.

1. Fifteen cases of staphylococcal pneumonia are described. They constituted approximately 3 per cent. of all pneumonias admitted to hospital.
2. In four patients the infection complicated epidemic influenza. All these patients had a very severe illness. One died, while the remainder had residual pulmonary fibrosis.
3. Penicillin therapy was successful in 40 per cent., but had to be replaced by streptomycin in 33 per cent. Aureomycin was used in 20 per cent., and it was curative in one patient whose disease was resistant to both the preceding antibiotics. It is probably the treatment of choice.
4. A serious complication is bronchial obstruction by thick tenacious sputum in debilitated patients. Indirect bronchial suction is indicated, and gave dramatic relief in three cases who appeared moribund.
5. The condition remains a serious illness, although the mortality has been greatly reduced by antibiotics. Six cases had some residual fibrosis or bronchiectasis. Two of these had further attacks of pneumonia within a few months.

It is a pleasure to record our thanks to Dr. V. D. Allison and Dr. N. Ainley for the bacteriology, Dr. H. McDowell for the radiological work, and to Drs. T. A. Kean and J. C. Davison for permission to publish some of the cases.

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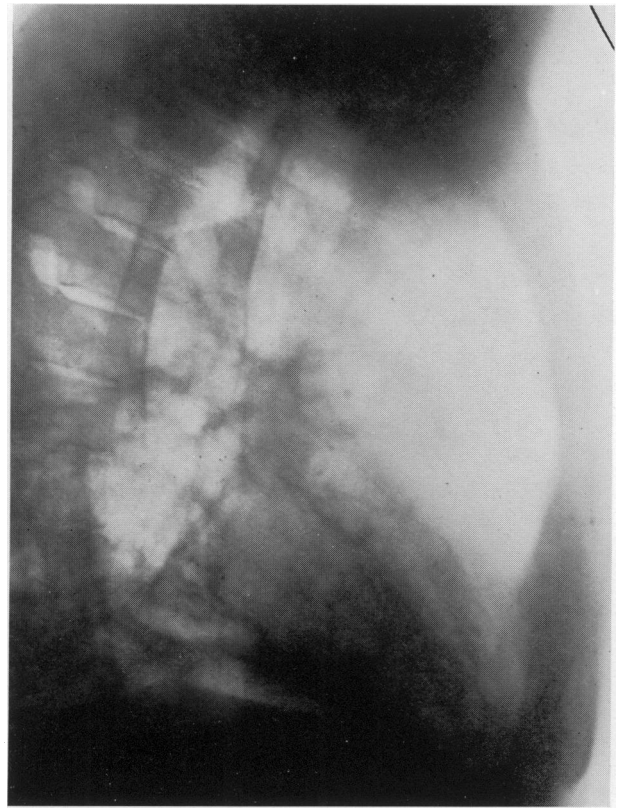
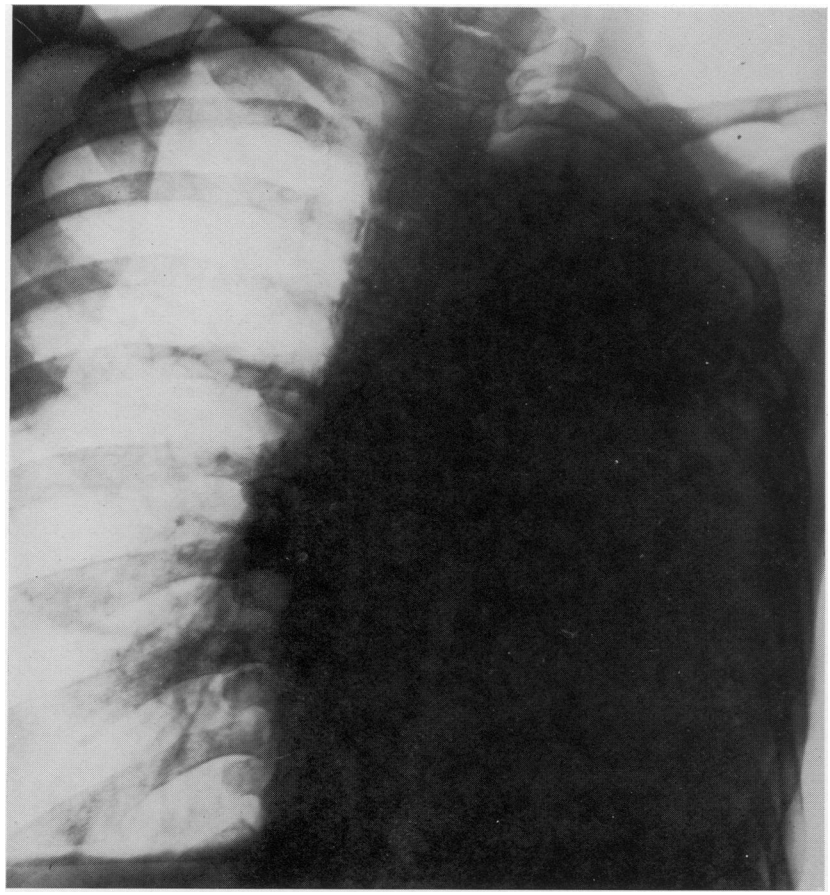


Film I.

Case 13.—Residual small cavities with surrounding fibrosis in left lower lobe.



Film II.

Case 14.—Fifteenth week. Collapse and consolidation of left lung.

Early Diagnosis and Treatment in Ankylosing Spondylitis

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THE neglected case of progressive ankylosing spondylitis is a tragedy. Like so many other disease processes, early diagnosis and appropriate therapeutic measures are essential if a satisfying result is to be obtained; particularly in this disease which is predominantly one of younger age groups. An analysis of a small series of patients, thirty-four in all, studied at the Northern Ireland Radiotherapy Centre, revealed the following facts :—

1. The average time between the onset of symptoms and the patient's reporting to his doctor was about six months.
2. The average time between the patient's reporting to his doctor and his coming for X-ray treatment was about six years.
3. In some cases the patient had had the disease for fifteen to twenty years before any treatment was given.

The results of X-ray therapy in these patients really provide no clue as to the response which should follow when the disease is recognised early and appropriate action taken. Were we to accept the results of treatment in this group as being typical, the outlook would indeed be pessimistic, for of all the patients only five have remained well, while twenty have relapsed and seven have failed to report. In the two others the time interval since treatment is so short that no accurate assessment can be made.

There is no known ætiology of the disease, except that one must presume it is the result of an obscure endocrine dysfunction, possibly of adrenal tissue. In the British Isles it is customary to look on ankylosing spondylitis as a separate disease from rheumatoid arthritis because of :—

1. Its different sex incidence, varying from 4-1 to 20-1 in favour of males. (Comroe, 1943.) (In this series of cases there were six female patients.)
2. The pattern of the joint involvement which is primarily centripetal.
3. The failure of response to gold therapy.
4. The good initial response obtained with X-ray treatment.
5. Ossification occurring in the late stages in the paraspinal structures, a condition rarely or never seen in rheumatoid arthritis.

It is, however, possible that ankylosing spondylitis and rheumatoid arthritis are related, as some cases of each respond well to treatment with A.C.T.H. and

butazolidin. In the different hormonal climates of the sexes it may be that a particular adrenal disorder produces a variation of disease pattern, so that spondylitis is seen predominantly in men and rheumatoid arthritis in women. The high incidence of ankylosing spondylitis in young Army recruits lends some support to the idea of a 'stress' disease.

The criteria for diagnosis are simple:—

1. A clinical history which suggests the disease.
2. An accepted joint distribution.
3. Radiological confirmation.
4. Raised B.S.R.
5. A negative gonococcal-complement fixation test.
6. Occasionally a serological test for abortus infection.

The last two tests are, in practice, rarely necessary.

The disease should be suspected in a young person, particularly a male, who complains of persistent or intermittent pain in the back. Most cases present as having low back pain and stiffness, worse after all forms of rest. Stiffness is an important symptom and should always be asked about. Other kinds of onset described are 'tired back,' twinges of pain in the buttocks, girdle pains, sore ribs, 'sciatica'—especially the alternating variety. Occasionally the disease begins with painful peripheral joints. In other cases the onset may be acute with fever, high sedimentation rate and severe pain. Such patients should be confined to bed till acute symptoms subside. Bed rest should always be minimal in all types of this disease.

On examination, one of the earliest signs is limitation of lumbar extension, and tenderness of the vertebral bodies to percussion is easily elicited. Limitation of other spinal movements occurs quite early in the course of the disease. Involvement of the neck with a short history is a bad prognostic sign. A raised B.S.R. is often seen even in chronic and subacute cases and denotes the continued presence of the disease. It may prove a useful sign if malingering is suspected. (Of course, a normal B.S.R. need not necessarily mean revision of the diagnosis.) "Poker back" is a late and irreversible stage of spinal involvement. In any atypical case, or where the X-ray findings do not agree with the clinical picture, enquiry should be made for a history of urethritis. A gonococcal-complement fixation test may be done or prostatic smear obtained, but these cases are extremely rare. Occasionally a serological test against abortus infection may be necessary, as this disease is thought by some to present infrequently with a syndrome like ankylosing spondylitis.

X-ray Findings.

These clinical findings can often be confirmed radiologically, but it should be remembered that sometimes X-ray changes do not appear for some months after the onset of symptoms. Patients with persistence of the above symptoms should be regarded as having ankylosing spondylitis and treated as such. Advanced X-ray

changes are of academic interest only, and the disease should not be thought of in terms of the "typical bamboo spine" which many people associate with spondylitis.

Careful examination of the sacro-iliac joints is essential, and these are best photographed with the tube at an angle of 30 degrees to the vertical plane and the patient recumbent, with the knees flexed. Early changes in these joints show a blurring of the subchondral lines, with a narrowing of the joint space. The whole joint space may be obliterated quite early. Sclerosis of bone occurs adjacent to the joint, and finally the whole picture proceeds to one of bony ankylosis. Sacro-iliac involvement is typically bilateral, and unilateral changes suggest tuberculosis or osteitis condensans ilii. Patchy demineralisation of bone may occur in the neighbourhood of the sacro-iliac joints and, in very severe and rapidly evolving cases, this change may be seen without any sclerosis. Occasionally sclerosis in the early stages is found in the caudal third of the sacro-iliac joints only.

The posterior articulations of the lumbar spine may be shown by three-quarter lateral views (Buckley, 1943) (Fig. 1). Very often these joints are affected early in the clinical course. Generalised rarefaction of the whole of the bony spine occurs in some early cases. 'Squaring' or 'sugar loaf' pattern of the vertebræ (Fig. 2), especially in the lumbar region, is quite often seen. A "compass" type curve is formed by the anterior bodies of the vertebræ in the thoraco lumbar-spine in certain cases (Fig. 3).

Treatment.

Once the disease has been diagnosed, treatment should be instituted without delay The patient must be made to realise that he has a serious condition which, if he neglects, may well cripple him, and that he must be prepared to devote a good deal of time and trouble to getting and keeping well.

Treatment can be divided into two stages, the first being X-ray therapy, and the second a prolonged period of active spinal and breathing exercises.

X-ray Therapy.

The initial treatment of choice is X-ray therapy. This should be given to the whole of the spine and sacro-iliac joints. (This refers, of course, to the majority of cases which commence with spinal disease.) The whole spine and sacro-iliac joints are treated in a block, as it has been shown by experience that, if an isolated region of the spine only is treated, pain will recur elsewhere. In addition, treatment of only part of the spine may allow changes to proceed in the unirradiated spinal and paraspinal structures to the patient's grave disadvantage, as he may have little pain till a stage of considerable disability has been reached. Initial treatment, therefore, should be adequate and, as far as X-rays are concerned, regarded as a once and for all treatment. Nothing is to be gained by waiting for pain to recur, as the whole aim of X-ray therapy is to stop the disease process.

In a young woman the sacro-iliac joints should not be irradiated, as sterilisation may be produced or a series of genetic mutations result. Fortunately, in a woman, the disease process is generally less severe, and tends to affect the thoracic and lumbar vertebræ. If, however, pain is severe in the sacro-iliac region, obviously treatment may have to be given.

Fig. 1.

Oblique view lumbar spine, demonstrating the posterior articulations of the lumbar vertebra.

Fig. 2.

Lateral view lumbar spine to show squaring or sugar loaf appearance in well-established ankylosing spondylitis.

Fig. 3.

Lateral view thoraco-lumbar spine to show the well-defined "compass" type of curve shown by the anterior surfaces of the vertebræ in moderately advanced ankylosing spondylitis.

Relief of symptoms after X-ray therapy is nearly always considerable, and very often dramatic. In this series fourteen patients had a good response, eleven had a fair response, and six could not be fairly judged, as they had insufficient therapy. These last were considered unsuitable for full treatment, being either too advanced or in too poor general health to have a complete course. It will be seen then that, although most patients had had the disease for a long time, the immediate response is quite good in a high proportion of them.

The response is always better where bad posture has not developed. Some authors have recommended that a spinal brace should be used, but experience gained in Edinburgh of many scores of cases of ankylosing spondylitis showed that spinal immobilisation appears useful only where there is very severe pain. Otherwise, immobilisation has everything to be said against it.

Exercises.

After X-ray therapy a proportion of patients remain free from pain without any further measures being taken. These are usually the early cases. Many of these are hard to follow up, as, being symptom-free, they do not see any necessity to attend hospital. A high proportion of patients, however, develop recurrence of symptoms even after X-ray treatment. Such symptoms may develop in the spine or in peripheral joints, such as the hip or shoulder or at muscular attachments. The group of patients who develop recurrence of pain in the spine is especially interesting. A critical evaluation of this group shows that most symptoms are due to poor posture, and it cannot be too strongly stressed that the help of the physiotherapist is necessary in every case of spondylitis which has had X-ray treatment. A patient should be told that, while he has obtained immediate relief, his pain is very likely to recur unless he is prepared to devote about half an hour a day to simple spinal and breathing exercises. He should also pay particular attention to exercises of his neck, as involvement of the cervical spinal joints is a very painful and incapacitating process. Neglect of breathing exercises and subsequent involvement of the costo-vertebral joints puts the patient on a path which leads to eventual chronic respiratory disease. Because of this, a patient should be made to develop pride in the amount of chest expansion he is able to attain.

The idea of active exercise should be conveyed to the patient in terms not of weeks but of years. A high proportion of patients in this series of cases relapsed, and in none of them could it really be said that any adequate subsequent spinal exercises had been carried out. Patients should sleep on a hard bed, if necessary placing boards below their mattresses. Very good and more interesting exercises are swimming and rowing. Lying on a hard floor, while very uncomfortable at first, is an excellent method of providing spinal extension. As this exercise becomes easier with practice, a pillow may be inserted under the lumbar region, and even two pillows, the aim being to secure perhaps an exaggerated degree of lumbar extension.

Relief from pain and good posture breeds confidence; many patients with ankylosing spondylitis really require psychological treatment. They have had

chronic pain for many years, so that they have become largely incapable of believing that it may ever disappear.

One further complication may be mentioned—iritis. It is not infrequent, and can be dramatically relieved by the use of A.C.T.H. eyedrops. Kling (1952) has reported good results in the treatment of spondylitis with butozolidin. As this is a dangerous drug, it should be reserved only for cases which are completely refractory to X-ray therapy; in addition the effect appears to last only as long as the drug is actually administered.

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REVIEWS

MODERN TREATMENT YEARBOOK, 1954. Edited by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., M.Ch., D.Sc., P.R.C.S. (Pp. viii + 352; figs. 69. 21s.) London: Ballière, Tindall & Cox, 1954.

THIS book of some 340 pages and 35 authoritative contributors is designed to keep the busy general practitioner up to date on the practical application of the latest research in diagnosis and treatment. As it endeavours to cover every branch of medicine, it is necessarily limited, and only those therapeutic methods which have been thoroughly tested and accepted are quoted. It is, in effect, an annual refresher course for general practitioners in book form, and, as such, should prove of inestimable value. W. J.

A HANDBOOK ON DISEASES OF CHILDREN, INCLUDING DIETETICS AND THE COMMON FEVERS. By Bruce Williamson, M.D.(Edin.), F.R.C.P.(Lond.). (Pp. 447; illustrations 103. 21s.) Edinburgh and London: E. & S. Livingstone, 1953.

THE latest edition of Dr. Williamson's handbook covers the essentials of modern pædiatric practice in a lucid and concise manner. With a few notable exceptions, recent advances in diagnosis and treatment are well presented. The problem of the wasted infant receives scant attention, and one would have expected some reference to current biochemical trends in the investigation of marasmus. The section on hæmolytic disease of the newborn is up to date, but few pædiatricians would favour the sagittal sinus as a route for replacement transfusion. The text is well set out and profusely scattered with excellent illustrations. On the whole, this handbook can be recommended to the general pracitioner as an informative reference volume. R. D. G. C.

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THE latest edition of Dr. Williamson's handbook covers the essentials of modern pædiatric practice in a lucid and concise manner. With a few notable exceptions, recent advances in diagnosis and treatment are well presented. The problem of the wasted infant receives scant attention, and one would have expected some reference to current biochemical trends in the investigation of marasmus. The section on hæmolytic disease of the newborn is up to date, but few pædiatricians would favour the sagittal sinus as a route for replacement transfusion. The text is well set out and profusely scattered with excellent illustrations. On the whole, this handbook can be recommended to the general pracitioner as an informative reference volume. R. D. G. C.

chronic pain for many years, so that they have become largely incapable of believing that it may ever disappear.

One further complication may be mentioned—iritis. It is not infrequent, and can be dramatically relieved by the use of A.C.T.H. eyedrops. Kling (1952) has reported good results in the treatment of spondylitis with butozolidin. As this is a dangerous drug, it should be reserved only for cases which are completely refractory to X-ray therapy; in addition the effect appears to last only as long as the drug is actually administered.

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REVIEWS

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Bacterial Endocarditis: The Process of Healing

By MARY GRAHAM MCGEOWN

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ALTHOUGH bacterial endocarditis has been recognised as a separate disease entity since Ormerod (1851) described the vegetations of bacterial endocarditis and showed how they differed from rheumatic verrucæ, several problems remain unsolved. Following the advent of the sulphonamide drugs and the antibiotics, the problems in connection with healing have become increasingly important. In the later 1940's the proportion of treated cases reaching a successful issue gradually increased, but failures still occur. A lack of careful preliminary bacteriological investigation and carelessness with the details of treatment would appear to account for some of the failures, but a considerable number remain unexplained. With these considerations in mind, it appears important to study the cellular process of healing.

MATERIALS AND METHODS.

The post-mortem records of the Institute of Pathology of Belfast, from January, 1938, to January, 1950, were used to provide material for this study. The series included both treated and untreated cases. As the treated cases did not differ greatly from the untreated ones, the stages of healing observed will be described, followed by a discussion of the effects of treatment.

Material from eighty cases was available for histological study. In the majority of instances, the blocks of the vegetations were recut, and in many cases sections at different levels were prepared. When signs of healing were present, serial sections at various levels were studied. The original sections were stained with hæmotoxylin and eosin, and where it was considered necessary this was supplemented by one or more of the following stains : a combination of Weigert's elastin stain with van Gieson's connective tissue stain; Masson's trichrome stain; Brown's modification of Gram's stain for bacteria; and von Kossa's stain for calcium.

RESULTS.

In the material of this study there were several examples of very early bacterial vegetations. These consisted of small masses of fibrin and bacteria, in which there were no traces of elastic tissue, situated directly on the surface of the valve. There was an early infiltration of inflammatory cells in the underlying valve. In larger vegetations the basal part of the lesions often contained strands of elastic tissue. It is thought that as the bacteria multiply, they ulcerate the substance of the valve, so that remnants of valve tissue come to be present in the basal part of the vegetation.

In the majority of these cases, bacteria could be identified in sections stained with Brown's stain. In a few cases in which the lesion was healing or healed, no

bacteria could be seen in the sections. The evidence will be presented for believing these cases to be examples of healed bacterial endocarditis.

Process of Healing. A proliferation of fibroblasts at the base of the vegetation was present to some degree in 63 per cent. of the cases studied. In those instances where there were well-marked attempts at healing, it could be seen that the proliferation of fibroblasts at the base, and especially at the margins, must have played an important part in the process of repair. It was sometimes present in early lesions, even in those which appeared otherwise destructive. It was present in vegetations from cases where the total duration of the illness had been less than three weeks, yet it was absent in one with an illness of three months. It was very marked in a case which had a perforation of the valve cusp. It was present to a marked degree in those cases where there was further evidence of healing.

This proliferation of fibrous tissue at the base of otherwise active vegetations was often accompanied by the formation of new capillaries, and, in some cases where healing was advanced, this was a prominent feature. Since fibroblasts were some times seen without recognisable capillaries, it was thought that the fibroblasts preceded the capillaries. Eventually a layer of granulation tissue was formed similar to that seen in association with inflammatory lesions in other parts of the body. When the vegetations were small, consisting mainly of fibrin, with few bacteria, it seems as though the advancement of this tissue gradually replaced the vegetation so that there remained only a pad of granulation tissue (Fig. 1). In several cases microscopic granulomata were seen on the heart valves and in the valve angles. Many hæmosiderin-containing macrophages were present in these lesions. There was no proof that they were of bacterial origin, but there was considerable evidence in support of this view. In one instance there were active bacterial vegetations on the other cusps of the valve. Lesions of this type have never been described as a result of rheumatism. They bear a close resemblance to bacterial lesions in other parts of the body.

This gradual replacement of the vegetation by granulation tissue did not appear to play a prominent part in the healing of larger vegetations. In such lesions the first important stage appeared to be the growth of endothelial cells from the adjacent endocardium over the surface of the vegetation. The endothelial cell layer was single at first and the cells were separated from the bacterial colonies by a layer of fibrin. In some cases this fibrin layer was very thin. This was present as early as twenty-three days after the onset of symptoms. The endothelial cells were derived from the adjacent healthy endocardium. They were large and active-looking, and spread gradually over the surface of the vegetation. Fibroblasts followed the endothelial cells over the surface of the lesion. This was usually, but not always, accompanied by the invasion of the base by fibroblasts. Various stages in the formation of a complete fibrous tissue capsule were seen. This process of encapsulation was sometimes present in lesions which were advancing in other areas. Bacteria which stained deeply with Brown's stain were occasionally present within completely encapsulated vegetations, showing that encapsulation can occur before the bacterial colonies are killed. In other lesions the centre consisted of necrotic material and

nuclear debris, without identifiable cells or bacteria. This process of encapsulation of the vegetation with fibrous tissue was considered to be an important stage of healing, as it indicated that the defences of the body were in the ascendant, even if only temporarily and locally.

Capillaries followed the fibroblasts over the surface, and eventually the vegetation became covered with a thick layer of granulation tissue, similar to that present at the base (Fig. 2). Hæmosiderin-containing macrophages were present within this capsule. Occasionally there were multi-nucleated giant cells of the foreign body type. In a few instances small masses of bacteria and fibrin, together with acute inflammatory cells, were seen beneath a layer of old collagenous fibrous tissue. The fibrous tissue was relatively acellular and was thought to be older than the bacterial lesion. This was considered to be the result of active bacterial lesions extending into an area of old fibrous thickening of the valve, and not a part of the process of repair.

There were numerous examples of partially and completely encapsulated vegetations. The centre of the vegetation was composed of necrotic inflammatory cells, dead and dying bacteria, and old fibrin. The necrotic material remained for a considerable time, and was sometimes present in lesions when collagen was present in the capsule. There were sometimes deposits of calcium in this core, even in relatively young lesions, when the bacterial endocarditis was advancing in neighbouring areas (Fig. 3).

These stages can be followed in vegetations where there is good evidence of bacterial origin. Bacteria can be identified even when calcification has commenced. Once the bacteria have disappeared we are faced with the problem of the interpretation of a scar. It is conjectured that the vascular channels gradually disappear and most of the hæmosiderin-containing macrophages are carried away in lymphatics. As this occurs, the scar loses its specific characteristics and becomes merely a mass of calcium buried in relatively avascular fibrous tissue. In this series there were three cases in which there were calcified vegetations of this type, associated with evidence which was strongly suggestive of bacterial endocarditis. There were several other cases in which histologically similar lesions were present, but without history or other evidence to suggest bacterial endocarditis. As their ætiology could not be decided, they have not been included in this series. Secondary calcification of an old area of rheumatic fibrous thickening of a valve cusp could produce an appearance similar to healed vegetations of bacterial endocarditis.

Examples of Healed Bacterial Endocarditis. Three male patients had a history of rheumatic fever many years before their final illness. In each case the streptococcus viridans had been isolated from the blood stream on two or three occasions. They improved with penicillin therapy, but after a period varying from six weeks to three and half years they died from congestive heart failure. At autopsy all had healed infarcts in the brain or abdominal viscera. There were healed vegetations on the mitral valve, in two cases associated with ruptured chordæ tendineæ. The larger vegetations consisted of masses of calcium buried in collagenous fibrous

tissue. In one case numerous blood vessels and crystals of hæmosiderin were present (Fig. 4). Bacteria were not present.

Effect of Treatment. In this series of cases twenty-nine received chemotherapy and/or penicillin therapy; forty-three cases were untreated; there was no information as to treatment in eight cases. The stages of healing which have been described can be found in the untreated, as well as in the treated cases, with the exception of the calcified scar. The more advanced stages of healing appeared more frequently amongst the treated cases, as one would expect, and the three cases which have been regarded as examples of completely healed bacterial endocarditis had received penicillin treatment. Healing tended to progress more rapidly in the treated cases, but even in these instances bacteria remained stainable within the vegetations for long periods. The difference between treated and untreated cases was not sufficiently striking to enable one to pick out the treated cases.

In both treated and untreated groups there was little relationship between the degree of healing and the duration of symptoms (the presumed age of the vegetations). Well-defined attempts to encapsulate the vegetations were seen in cases with symptoms for twenty-three and thirty-five days respectively, although no treatment with sulphonamides or penicillin had been given. A treated case with symptoms for thirty days had similar partially encapsulated vegetations. In another untreated case this process was only beginning after six months.

Bacteriology. A micro-organism was isolated in thirty-five of the eighty cases studied. In twenty-five cases the organism was recovered from the patient's blood stream during life. In eight cases bacteria were cultured from the vegetations and/or the spleen at post-mortem. However, Wright (1925) and Epstein and Kugel (1929) regarded post-mortem cultures as of doubtful significance. The latter workers isolated streptococci in 40 per cent. of cultures taken from normal valves.

In only two cases in the present series was the same organism recovered at post-mortem as had been obtained by blood culture during life. The Streptococcus viridans was isolated in eleven cases, the Staphlococcus aureus in ten, the Staphlococcus albus in three, the Streptococcus hæmolyticus in three, the Hæmophilus influenza in three, and the Pneumococcus in five.

When the degree of healing was compared with the casual organism, it was interesting to note that, in general, there were few or only slight signs of healing in the vegetations due to pyogenic organisms. Occasionally, however, a vegetation from which a pyogenic organism had been isolated showed more advanced healing than some of the vegetations due to the Streptococcus viridans.

Discussion.

It will be noticed that there has been no attempt to classify this series of cases into acute and subacute bacterial endocarditis. It was found unreliable to divide the cases into these two types on a basis of duration of symptoms, especially as the disease has typically an insidious onset. In some instances patients died from embolization or intercurrent infection early in the course of the disease, yet histological examination of the vegetations revealed well-marked proliferation of

fibrous tissue at the base and attempts to cover the surface. On a basis of time alone, these cases would have been classified as examples of acute bacterial endocarditis. It seems unsound to regard as subacute all those cases where the endocarditis appears to be the primary infection, and to reserve the term acute for those in which a primary infective process has been found in another organ. Cases were examined where the vegetations were of the destructive ulcerative type, yet no other infective process was found. Healing vegetations were seen in a case where the endocarditis was a secondary lesion. It was concluded that the disease should be called bacterial endocarditis, adding the name of the casual organism, where it is known, as a prefix.

The Healing of Bacterial Vegetations. The first favourable reaction of the valve to the presence of the bacteria, apart from an infiltration by inflammatory cells, appears to be a proliferation of fibroblasts at the base of the vegetation. It was present in 63 per cent. of the cases studied, but in the majority of them the attempt to heal the lesion had not proceeded further. In most instances it appeared as though the body's defence mechanism was unable to hold the infection in check while the process of healing continued. Some times a cerebral embolus or an episode of intercurrent infection terminated the life of the patient. The presence of fibroblastic activity did not appear to be related to the duration of the symptoms (although this appears to be an unreliable criterion for the age of the infective process, since the disease is notoriously of insidious onset). It was present in a number of cases which had not received chemotherapy or antibiotic treatment. It was impossible to exclude a varying degree of virulence of different organisms, or even of different strains of the same organism, but even this factor did not appear to account for its presence or absence. Occasionally a vegetation from which a pyogenic bacterium had been isolated showed more advanced healing than some of the vegetations due to the streptococcus viridans. It was thought that the importance of the fibroblastic proliferation lay in the fact that it showed that the patient had the power to react to the bacterial process. More extensive repair might have been achieved if the patient had survived for a longer period.

The first definite stage of healing appeared to be the proliferation of the cells of the healthy endocardium adjacent to the vegetation. These cells extended over the vegetation on a layer of bacteria-free fibrin, which formed the periphery of the vegetation. The endothelialization of a bacterial vegetation is of great importance in the process of healing. As long as the vegetation remains in open communication with the blood stream, the fibrin portion of it offers an ideal culture medium for bacteria carried to it by the blood stream. Even if the interior of the vegetation becomes sterile, the outer surface remains adhesive, so that chance bacteria might easily adhere to it and give rise to a fresh episode of infection. With the formation of a smooth endothelial covering, the adhesiveness disappears, and there is a consequent decrease in the danger of reinfection. Treatment ought to be continued at least until the surface of the vegetation is completely covered with endothelium.

The formation of a fibrous tissue capsule by the growth of fibroblasts following the endothelial cells over the surface of the vegetation appears to be the next stage

of healing. Capillaries followed the fibroblasts to form a capsule of young granulation tissue. It was interesting to observe that one part of a vegetation might be covered in this way, while the bacteria were advancing in a neighbouring area. Nevertheless, there were some vegetations in which the bacteria appeared to be non-viable in some areas (as judged by post-mortem culture and staining reactions), yet no attempt to cover the dead colonies had occurred.

As the fibrous tissue capsule was forming, fibroblasts were growing into the base of the vegetation, anchoring it firmly to the valve. The possibility of fragments of the vegetation becoming detached and the formation of emboli were more remote. There was no significant difference in the occurrence of embolization in the treated and untreated cases in this series.

After the vegetations had become encapsulated, the bacteria tended to lose their staining reactions, and were considered to be no longer viable. It was noteworthy that this stage might be delayed until the capsule had become adult fibrous tissue, and most of the inflammatory cells had disappeared. The long survival period of bacteria within healing vegetations has an important bearing on the time for which treatment should be continued. As long as bacteria which stain well remain within the vegetation, a recrudescence of infection may be possible, and treatment should be continued until this danger is past. Christie (1948) reported deeply staining bacteria in the vegetations of thirteen out of thirty-nine apparently controlled cases. Knowledge of this does not help in determining the duration of treatment in the individual patient, but it indicates that a prolonged course of treatment would be more likely to give good results than a short course however high the dosage. This is in agreement with the findings of clinical investigators (Christie, 1948; Donzelot, Kaufman and Escalle, 1947).

The mass of material forming the core of the encapsulated vegetation, consisting of necrotic material and dead bacteria, appeared to shrink a little and calcium salts were deposited within it. It is interesting to note that this sometimes occurred even in vegetations in which the bacteria still stained deeply, and there were numerous polymorphonuclear cells in the surrounding fibrous tissue. Once the centre of a bacterial vegetation becomes infiltrated with calcium, the shape and the size of the scar is fixed, and if it is large there results a considerable deformity of the valve on which it is situated. In very small vegetations the advance of granulation tissue from the base appears to replace the vegetation without the deposition of calcium salts, presumably because the amount of necrotic material is small and can be carried away by phagocytes. Where there is a large mass of necrotic material, only the fringe of it is accessible to the action of the phagocytic cells. The replacement of the vegetation by granulation tissue ought to result in less deformity of the valve cusps. From a pathological point of view, as well as a clinical one, early diagnosis and treatment, while the vegetations are still small enough to be healed in this way, seems to be essential to obtain a good functional result.

Some of these stages of healing have been described by other workers. Libman (1912) described masses of calcium embedded in relatively avascular fibrous tissue

situated on the heart valves. They were associated with healed perforations of the cusps and with healed Lohlein's lesions in the kidneys, and he believed them to be examples of healed bacterial endocarditis. Moore (1946) studied the healing process in cases of bacterial endocarditis which had been treated with penicillin, and he described the covering of the vegetations with fibrous tissue, and the partial removal of the necrotic material by phagocytes, followed by the deposition of calcium salts in the remaining necrotic material. He described a final stage in which clefts appeared in the vegetation and became lined with endothelium, to form a spongework of blood channels, which he considered was pathogonomic of bacterial endocarditis. This spongework was not seen in the material forming the present study. His study was carried out on twenty-two treated cases of bacterial endocarditis, with eight untreated cases as controls. He found some evidence of healing in the control cases, but it was more advanced after treatment with penicillin.

From the present study it appeared that the most important factor influencing the degree of healing was neither the age of the lesion nor the treatment received. The micro-organism causing the disease appeared to be of great importance apart from differences in sensitivity to chemotherapy and antibiotic treatment. If the organism was of sufficient virulence, then the patient died early in the course of the disease, and the treatment did not appear to affect the issue. In the group of cases which survived longer, usually due to the Streptococcus viridans, there were widely differing stages of healing. It was thought that this could only be accounted for by assuming some differing power of tissue response in the individual patient. Many factors might influence the tissue response, for example, the state of nutrition of the patient and the effect of bacterial toxins from the heart lesion. In the present state of our knowledge it would appear that general measures of good nursing and attention to the state of nutrition of the patient still have an important place in the treatment of bacterial endocarditis.

Summary.

1. The findings of a study of eighty cases of bacterial endocarditis have been described.

2. The healing of bacterial vegetations occurs in the following stages :—
   - I. Invasion of the base by fibroblasts and young capillaries.
   - II. Endothelialization of the surface.
   - III. Formation of a fibrous tissue capsule.
   - IV. Death of bacteria.
   - V. Calcification of the necrotic centre of the vegetation.

3. It is suggested that the accepted classification of bacterial endocarditis into acute and subacute types does not serve any useful purpose, and it is proposed that the disease should be called bacterial endocarditis, qualifying this where possible with the word healing or healed, and the name of the casual organism.

4. The treated cases are compared with the untreated, and it appears that while the healing may be facilitated by treatment, the essential nature of the process of healing is not altered.

5. There is no apparent relationship between the presumed age of the vegetation and its histological appearance.

6. Less advanced healing, in general, occurred in vegetations due to pyogenic organisms, while healing had progressed further in those due to the Streptococcus viridans.

7. It is suggested that the tissue response of the individual has an important bearing on the degree of healing achieved. This might be influenced by the state of nutrition of the patient, and by bacterial toxins produced by the bacteria causing the disease.

8. It is essential to diagnose and treat bacterial endocarditis while the vegetations are still small, if a good functional result is to be obtained. Treatment should be very prolonged since apparently viable bacteria can persist for long periods in the middle of healing vegetations.

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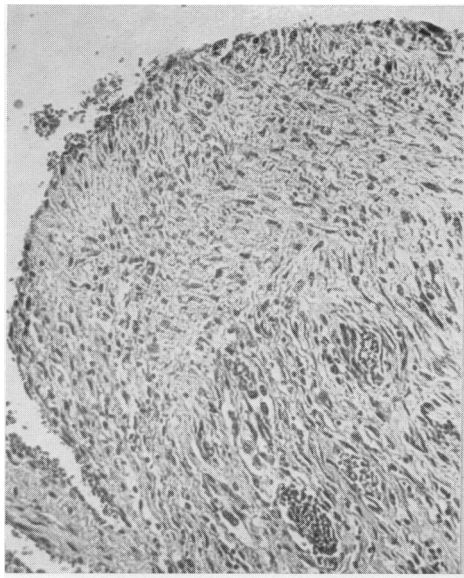

Fig. 1.

A 6612 H. and E. ×140.
Microscopic granuloma in the mitral valve angle.

Fig. 2.

A 3154 H. and E. ×92.
Thick layer of granulation tissue covering a bacterial vegetation.

Fig. 3.

A 6530 H. and E. ×140.
Calcium in vascular granulation tissue at the base of a bacterial vegetation.

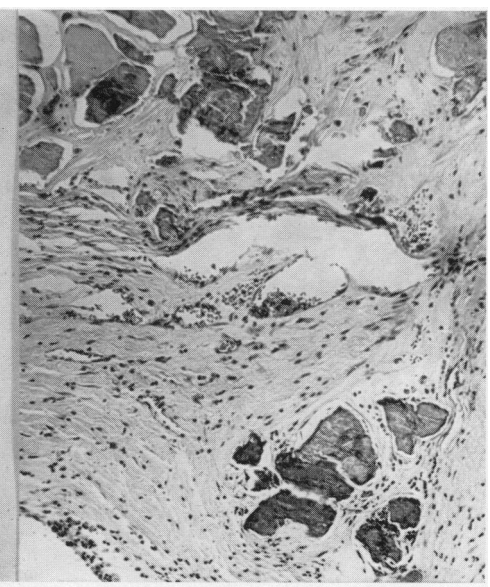

Fig. 4.

A 6242 H. and E. ×90.
Masses of calcium, embedded in fibrous tissue—completely healed bacterial endocarditis.

The Clinical Diagnosis of Multiple Myeloma

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MULTIPLE myeloma is often looked upon as being a rare disease, but there is reason to believe that this is not so. During a period of forty-one months, eight cases of multiple myeloma were admitted to the adult general medical wards of the Belfast City Hospital. In the table below the occurrence of multiple myeloma is compared with that of a number of well-known hæmatological conditions admitted during this time.

DISEASE.	NUMBER OF CASES ADMITTED.
Multiple myeloma	8
Leukæmia (all varieties)	23
Hodgkin's disease	16
Reticulosis	6
Lymphosarcoma	1
Polycythæmia vera	1
Pernicious anæmia	92

These figures show that multiple myeloma occurs with about one-half the frequency of Hodgkin's disease and about one-third that of the leukæmias in the admissions to this hospital.

Multiple myeloma has the synonym of Kahler's disease as it was described by Kahler in 1889. Several accounts had appeared in the British literature many years before this date. Geschickter and Copeland compiled a review of all the published cases up to 1928. Since then several other reviews have appeared, including those of Atkinson (1937), Stewart and Weber (1938), Bayrd and Heck (1947), and Lichtenstein and Jaffé (1947).

PATHOLOGICAL FEATURES.

The essential lesion in multiple myeloma is a proliferation of plasma cells in the bone marrow. This occurs in those bones which contain red marrow and so the vertebræ, ribs, sternum, skull, pelvis, and the upper ends of the humerus and femur are the bones most often affected. The plasma cell is a little larger than a lymphocyte, and is distinguished by its cytoplasm, stained deep blue with Leishman's stain, and by the situation of the nucleus at one side of the cell. The strands of chromatin in the nucleus are arranged in a radial or spoke-like form. Larger cells, with very abundant cytoplasm and often containing two or more nuclei, occur in the lesions. These are usually regarded as abnormal varieties of plasma cell. The origin of the plasma cells and their function is still controversial. They constitute up to 1 per cent. of the nucleated cells present in normal bone marrow (Israëls, 1948). The proliferation of plasma cells may range from a single

tumour nodule in one bone to a diffuse infiltration not only of the entire red marrow, but involving the liver, spleen, lymph nodes, tonsils, kidneys, thyroid, pancreas, and heart. Between these two extremes all degrees of plasma cell proliferation and invasion are found. In many cases of multiple myeloma a few plasma cells escape into the circulating blood. In cases where the lesions are very widespread, large numbers of plasma cells appear in the peripheral blood. It is to these cases that the name plasma cell leukæmia is applied. (Patek and Castle, 1936.)

Examination of the sternal marrow by aspiration or actual biopsy is a very valuable diagnostic procedure. In multiple myeloma the marrow shows an increase in plasma cells of all varieties. Up to 90 per cent. of the nucleated cells may be of the plasma cell type in some cases, but in more than half of the patients only a moderate increase is present. A small increase in plasma cells occurs in Hodgkin's disease, marrow secondaries, and in hypoplasia of the marrow. (Israëls, Leitner, 1948.) In cases where there is patchy distribution of the lesion, the sternal marrow may be normal in appearance. Puncture of the sternum at another site, or aspiration of the iliac crests, vertebral spines or ribs will usually reveal an increase in plasma cells in these cases. (Beizer, *et al.*, 1942.) ...

The pathological process in the marrow can often be revealed by X-ray examination. The involved bones show many small clear areas, up to 1 cm. in diameter, with well-defined edges, giving them the appearance of having been punched out of the bone. In cases where the infiltration is very diffuse, there is often a generalised rarefaction of the involved bones. The cellular proliferation in the bone marrow leads to a weakening and an increased liability of the affected bones to injury. Pathological fractures, especially of the ribs and collapse of the vertebral bodies often occur.

It will be apparent that extensive plasma cell proliferation in the marrow will interfere with erythropoiesis and produce some degree of anæmia. The leucocyte formation may be upset, in some cases resulting in a leucocytosis or a leucopenia.

Disturbances of Protein Metabolism.

A strange feature of this plasma cell proliferation in the marrow is its influence on the proteins of the blood. This phenomenon is not observed in every case. The effect on the blood proteins is threefold; first, there is an increase in the total protein content of the plasma, giving levels from 8 to 15 grms. per 100 ml. and even as high as 20 grms. per 100 ml.; second, this increase is due to a marked rise in the globulin fraction of the plasma, resulting in a reversal of the albumin-globulin ratio which may be extreme in some cases; third, an abnormal protein may be present in the plasma. It is a globulin and has the property of solidifying on exposure to cold. This is readily demonstrated by removing the cells in a warm room and allowing the plasma to cool in the refrigerator. A solid, jelly-like substance appears in the tube. The name cryoglobulin is applied to this peculiar protein, and it is only present in a few cases of multiple myeloma (Blades, 1951).

In some cases, especially those where there is a disturbance of the blood proteins, the red cells exhibit a tendency towards excessive rouleaux formation and clumping. Under such circumstances accurate red cells counts are difficult to perform. An

important consequence of this excessive rouleaux formation is the increased sedimentation rate of the red cells in cases of multiple myeloma. One observer has actually witnessed this clumping of the red cells in the retinal vessels through the ophthalmoscope. (Foord, 1935.)

When the acidified urine from a case of multiple myeloma is warmed to about 50°C., a cloud appears. If the heating is continued to boiling point, this cloud disappears. On cooling the urine, the cloud reappears. This cloudiness is due to the presence of a substance known as Bence-Jones' proteose. It is not found in the urine of every case and, when present, the amount excreted varies greatly from day to day. The origin of this substance is uncertain and its relationship to the altered blood proteins has not been established. In some patients, who are excreting large amounts of Bence-Jones' proteose, there is interference with renal function, and death in uræmia may occur.

Clinical Features.

The majority of patients are over 40 years of age, with the peak incidence at 55 years. (Whitby and Britton, 1950.) More males are affected than females.

The lesions are situated in the bones, hence pain, tenderness, and pathological fracture are the chief clinical features. There is usually some emaciation and anæmia present. These symptoms will be considered in more detail in the discussion on diagnosis.

The prognosis of multiple myeloma is poor, the duration of most cases being measured in months.

No treatment has any influence on the disease process. Stilbamidine (Propp, 1949) and Urethane (Nelson, 1952) are of value in giving symptomatic relief, especially if administered early in the disease.

Clinical Summaries.

Case No. 1.—W. McC., male, aged 68 years. History of severe shooting pain down the back of the right leg and pain in the low back for eight months, unrelieved by physiotherapy. No loss of appetite or weight. On examination, healthy-looking, elderly man, afebrile and showing no physical signs other than tenderness over the upper end of the right femur. Investigations—Hb. 70% (Haldane), W.C.C. 5,400/cub. mm., film normal; urine—trace of albumin, no Bence-Jones' proteose detected; blood proteins—total 8.8 g. %, albumin 3.6 g. %, globulin 5.2 g. %; sternal marrow 21% plasma cells. X-ray—multiple translucent areas in the ribs and pathological fractures of the right sixth and seventh ribs and collapse of the bodies of T.7 and L.1 and L.2. No response to urethane treatment.

Case No. 2.—M., G., female, aged 65 years. History of pain in the lumbar region, radiating into the shoulders and abdomen, present for twelve months. It is increased by coughing and sudden movement, and is relieved by resting. No loss of appetite or weight. On examination, obese elderly woman, afebrile and exhibiting only tenderness over the fourth ribs anteriorly. Investigations—Hb. 90% (Haldane), W.C.C. 3,200/cub. mm., normal film, B.S.R. 25 mm./hr.; urine—no albumin or Bence-Jones' proteose detected; blood proteins—total 6.5 g. %, albumin 5.6 g. %, globulin 0.9 g. %; sternal marrow 32% plasma cells. X-ray—the lumbo-sacral spine, ribs, and pelvis show multiple small clear areas, with collapse of the bodies of T.10 and 12 and L.1.

Case No. 3.—L. N., female, aged 50 years. History of pain in the small of the back, increased by coughing and sneezing and present for one month, accompanied by some loss

of appetite. On examination, anæmic, middle-aged woman, afebrile, with tenderness present over the lumbar spine. Investigations—Urine : no albumin or Bence-Jones' proteose detected; blood proteins—total 7.5 g. %, albumin 3.0 g. %, globulin 4.5 g. %; sternal marrow 22% plasma cells. X-ray ribs and skull show multiple small translucencies. Stilbamidine produced symptomatic improvement.

Case No. 4.—E. N., female, aged 30 years. Admitted to hospital for the investigation of a respiratory catarrh, no history of pain. On examination, well-nourished woman, afebrile, showing only marked tenderness over the fifth left ribs anteriorly. Investigations—Hb. 64% (Haldane), W.C.C. 7,200/cub. mm.; film normal; B.S.R. 144 mm./hr.; urine—no albumin or Bence-Jones' proteose detected; blood proteins—total 12.8 g. %, albumin 3.2 g. %, globulin 9.6 g. %; sternal marrow 34% plasma cells. X-ray chest—fifth and sixth left ribs, sixth and eighth right ribs, lower end of the sternum, the skull, pelvis, the right humerus and femur show multiple small clear areas.

Case No. 5.—P. McP., male, aged 47 years. History of severe pain in the chest and upper abdomen, radiating round both sides from the back, and increased by twisting movements, duration eight months. Also marked loss of appetite and weight, together with progressive weakness. On examination, fairly well-nourished man, afebrile, with considerable tenderness over the left lower ribs, the sternum and the skull. Investigation—Hb. 78% (Haldane), W.C.C. 12,200/cub. mm., film normal; B.S.R. 90 mm./hr.; urine—no albumin or Bence-Jones' proteose detected; blood proteins—total 5.5 g. %, albumin 3.2 g. %, globulin 2.3 g. %; sternal marrow biopsy—"Myeloma"; X-ray—multiple small translucencies in skull and lumbar vertebræ. The response to urethane treatment was very poor.

Case No. 6.—M. H., female, aged 46 years. Admitted as a case of anæmia for investigation. No history of pain. On examination, anæmic woman, fairly well-nourished, afebrile, no physical signs other than slight enlargement of the liver and spleen. Investigations—Hb. 48% (Haldane), macrocytic anæmia, W.C.C. 4,300/cub. mm., film normal; B.S.R. 73 mm./hr.; urine—albumin +++, Bence-Jones' proteose present; blood proteins—total 11.0 g. %, albumin 2.4 g. %, globulin 8.6 g. %; sternal marrow 17% plasma cells; X-ray reports not available.

Case No. 7.—R. F., male, aged 53 years. History of severe pain and swelling in the region of the left hip. Increased by walking and unrelieved by analgesics. Loss of appetite and weight, duration twelve months. On examination, large bony swelling in left iliac crest, no tenderness, normal range of movement in left hip joint, enlarged lymph nodes in left groin. Investigations—Hb. 57% (Haldane), W.C.C. 4,700/cub. mm.; B.S.R. 22 mm./hr.; urine—no albumin or Bence-Jones' proteose detected; blood proteins—total 7.2 g. %, albumin 4.0 g. %, globulin 3.2 g. %; blood urea 22 mgms. %; sternal marrow—"Numerous plasma cells are present." X-ray shows destruction of left ilium.

Case No. 8.—M. F., female, aged 74 years. History of severe knife-like pains in left lumbar region and right sub-costal region for seven months, also loss of appetite and weight. On examination, poorly nourished elderly woman, afebrile, mildly anæmic, tenderness in the left lumbar region. Investigations—Hb. 63% (Haldane), W.C.C. 10,900/cub. mm., film normal; B.S.R. 153 mm./hr.; urine—a trace of albumin present, but no Bence-Jones' proteose detected; blood proteins—total 9.5 g. %, albumin 3.0 g. %, globulin 6.5 g. %; sternal marrow 45% plasma cells; X-ray lumbar vertebræ, ribs, pelvis, and skull show many small areas of translucence. No response to urethane treatment.

Diagnosis.

In this small series of cases, the average period of time elapsing between the onset of symptoms and the making of the diagnosis was seven and a half months. In Geschickter and Copeland's series of cases it was seventeen months, in Lichtenstein and Jaffé's series it was nine months, and in Propp's series six months. There are at least two reasons for this delay in diagnosis. The first reason is that during

the early stages of the disease, when the symptoms are mild and the disability trivial, patients may be reluctant to seek medical advice. The second reason is a failure to recognize the disease early in its course. The practitioner can do very little about the first reason, although more and more patients are consulting their doctors about trivial complaints. The remedy for the second reason lies with the practitioner. Some may argue that the early diagnosis of an incurable disease is unimportant. This is not so, because the two drugs, stilbamidine and urethane, act best in the early stages of the malady.

The commonest presenting symptom is pain. This pain in over one-half of cases is located in the back and in over one-quarter is situated in the chest or abdomen, while some patients only experience pain in the limbs. A few may have no history of pain (cases 4 and 6). The pain is usually of an aching or stabbing character and may be very severe. It is often aggravated by movement, by coughing, and is eased by rest. Haggart and Copel (1953), in a recent paper on the early diagnosis of bone tumours, stress the importance of pain which occurs and persists when the patient is at rest. Pain at night may occur. Simple analgesics and physiotherapy give more relief in benign rheumatic conditions than in multiple myeloma. A poor response to these simple measures should arouse the suspicion of a more serious disease.

Pains due to involvement of nerve roots by collapsed vertebræ may be present. These include "girdle pains," "sciatica," and other root pains, together with muscular wasting, loss of tendon reflexes and sensory impairment in the area supplied by the affected nerve.

The accompanying complaints of loss of appetite, loss of weight and of weakness and pallor are significant. They are seldom encountered in benign muscular conditions.

The most important physical sign is tenderness over the affected bones; this tenderness occurs in the absence of pathological fracture. In six of the present series of cases it was present, and its importance is emphasized by the various reviewers. The presence of bone tenderness in a patient complaining of vague pains and aches is suggestive of a serious lesion. It may be the only physical sign present, as in case 4, where it gave the clue to the diagnosis. A careful search should be made for its presence in all cases of "rheumatism," particularly over the ribs, vertebral spines, sternum, pelvis, and skull. In seeking for spinal tenderness, the "anvil" test is sometimes of value. The patient is seated upright and the crown of the head is percussed by the examiner's clenched fist. Pain is experienced over the diseased vertebra when the test is positive. It is also applicable in the detection of lesions in the pelvis or femur close to the hip joint. This time the patient is recumbent, the leg, with the knee fully extended, is raised to about 30°, and the heel is percussed with the examiner's fist. Pain is felt in the region of the hip joint when the test is positive.

Pathological fracture was present in only one patient in this series. Most reviewers regard it as a common finding. Hunter (1950) states that in no other tumour does pathological fracture occur so frequently. It may occasionally be the

presenting symptom. Enlargement of the liver, spleen, and superficial lymph nodes is so infrequent as to be of little value in diagnosis.

When confronted by a patient complaining of aching pains in the back, chest or limbs, with some emaciation and pallor and exhibiting bone tenderness, consideration should be given to investigating the possibility of multiple myeloma or other bone tumour, rather than ordering salicylates and physiotherapy. Three simple tests, well within the scope of any surgery, should be performed on all suspicious cases.

The first is the testing of the urine for albumin, and while the test-tube of acid, or if necessary acidified, urine is being gradually warmed, a careful watch is kept for the appearance of a cloud of Bence-Jones' proteose at a temperature well below boiling-point. Albumin may be present as well, but does not appear until boiling-point is reached. This test is best carried out in a simple water-bath over a small flame. Such a bath is easily improvised from a small saucepan or enamel mug. The presence of Bence-Jones' proteose will clinch the diagnosis. Various authors report it present in 30-60 per cent. of cases. Only one patient in the present series was found to be excreting it. Its absence does not exclude multiple myeloma.

The second test is the estimation of the hæmoglobin, usually by Sahli's method. Some degree of anæmia is nearly always present, and it may be quite severe. In case 6 it was the presenting symptom and the diagnosis was only made after routine sternal puncture.

The third, and perhaps the most important procedure, is the estimation of the blood sedimentation rate (B.S.R.). This is easily done by the well-known Westergren method. It is almost invariably raised above the normal rate of 3-5 mm./hr. for males and 4-7 mm./hr. for females in multiple myeloma and a diagnosis of "muscular rheumatism" should not be made when the B.S.R. is raised. Many distinguished reputations have been saved by doing the B.S.R. in patients complaining of vague aches and pains due, not to neurosis, but to multiple myeloma or other serious disease. It was elevated in six out of seven of the present series of patients.

The results of these simple tests, together with the history and clinical findings, should enable the practitioner to decide fairly shrewdly whether the patient's pains and aches are due merely to "rheumatism" or to a more grave condition of the bones. At this stage, arrangements can be made for the performance of the more specialised procedures, including estimation of blood proteins, radiology of the bones and sternal puncture.

Differential Diagnosis.

Hyperperathyroidism and osteomalacia can produce symptoms resembling those of multiple myeloma. These include pain and tenderness in the bones and sometimes pathological fracture. It is important to distinguish these two diseases from multiple myeloma, because of the difference in prognosis. Hyperparathyroidism is amenable to the surgical removal of parathyroid tissue and osteomalacia is cured by vitamin D therapy. In these two diseases there is very gross deformity of the affected bones and the X-ray appearances are different. The absence of plasma

cell proliferation in the sternal marrow serves to distinguish these two diseases from multiple myeloma.

Multiple myeloma may be simulated by widespread secondary tumour deposits in the bones. When the primary growth is not obvious, the clinical diagnosis is difficult. Recourse is usually made to the X-ray appearances, the blood proteins, and the sternal marrow in distinguishing between these two conditions.

Summary.

The eight cases of multiple myeloma reported occurred in forty-one months, and compared with other hæmatological conditions, it is half as frequent as Hodgkin's disease and one-third as frequent as leukæmia.

Attention is drawn to the delay of many months before the diagnosis is made in the majority of cases.

Pain is the predominant symptom, and especially significant is pain at rest, together with tenderness over the affected bones.

Examination of the urine for Bence-Jones' proteose and estimation of the hæmoglobin level and blood sedimentation rate are of value in distinguishing multiple myeloma from the benign rheumatic conditions.

The author wishes to thank the visiting physicians for permission to publish these cases. The sternal punctures were performed by Dr. Lewis. Dr. McKeown reported the sternal biopsy on case 5. The X-ray reports are those of Dr. McDowell. The Medical Records Officer supplied the details of the admissions. Case 4 was treated with urethane by Dr. Nelson and is reported elsewhere.

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Recording Genetic Information Concerning Individuals and Families

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THE notes which follow are intended to form a convenient source of reference for clinicians and others who encounter individuals and families with interesting variations and traits. As specific abnormal traits are usually uncommon and are seldom encountered, the individual clinician may have to spend much time searching for guidance on what information he should collect which may be relevant to the genetical interpretation of his observations.

The basic mechanisms of elementary genetics are readily understood and accounts may be found in any text-book. However, in man, where families are small, generations alive at one time few, and experiment impossible, the recognition of a genetic mechanism may be very difficult. It follows that increases in genetic knowledge from clinical and family pattern studies will usually come from descriptions and data from many sources. Such descriptions and such data must therefore be as accurate and as detailed as possible if the maximum contribution to knowledge is to be made.

Not infrequently reports of genetic interest omit many simple facts about the patient or family which are readily available, but were either not elicited or not recorded because their importance was not realized. Usually the intention of the recorders is to look for evidence which will enable the type of inheritance to be recognised. In essence this involves comparison of the observed pattern of a trait in a family or families with that to be expected on various theoretical hypotheses. If there are gaps in recorded information about affected and, equally important, unaffected members of the families the observed patterns will be distorted and misleading.

In brief, the following information is required about the person whose condition initiated the family study (the "Propositus" or "Index Case" or "Proband") and about each of his relatives living and dead.

1. Relationship to propositus.
2. Sex.
3. Whether alive or dead, and if dead, date and cause of death.
4. Age, or preferably date of birth—certainly age with sufficient accuracy to establish birth rank in a sibship.

5. Whether seen or not seen by the clinician and whether or not examined by him or by colleagues.
6. If not seen, the reasons.
7. Whether or not affected—if affected then adequate clinical notes.
8. If affected, the age of onset of the condition or the age when first recognised.
9. Other abnormalities or specific traits observed.
10. Specimens should be obtained for
    (*a*) blood grouping—complete "genotyping."
    (*b*) salivary secretion of A or B Group antigens.
11. Tests should be made for
    (*a*) colour vision.
    (*b*) ability to taste 20 pts. per million phenylthiocarbamide.

For each family as distinct from individuals in the family a record should be made of:—

(1) Consanguinous marriages.

(2) Multiple births.

(3) Miscarriages and fœtal deaths.

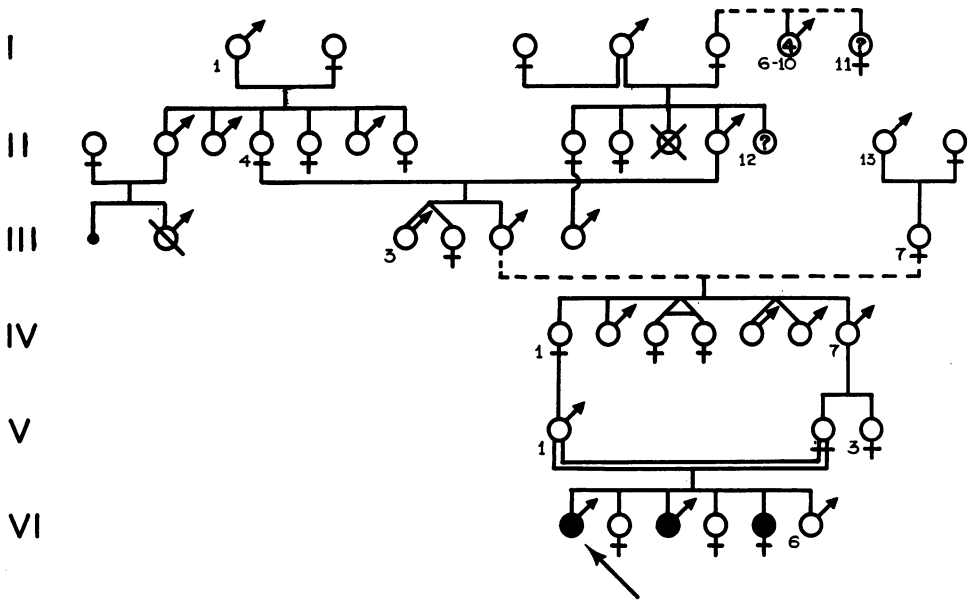
The above items, while perhaps serving as a rapid source for checking that essential information is being collected, require some justification and elaboration.

Mentioning the need for adequate clinical description (7) may seem unduly pessimistic, and even insulting to readers, but it should be remembered that expression of the same gene may vary considerably in different individuals and that the expression of different genes may at times be very similar so that only good clinical notes and clinical pathological records may enable other readers to identify the condition for comparison with their own observations or with those described by other authors. Only then can geneticists assemble with confidence sufficiently large series of cases or families to permit genetical interpretation. The modes of inheritance of retinitis pigmentosa and of muscular dystrophy are but two examples of conditions where inadequate clinical descriptions have been misinterpreted with unfortunate results.

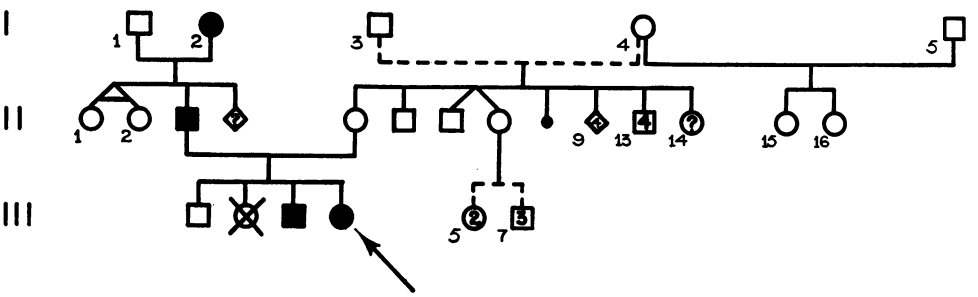
The importance of seeing as many members of the family as possible (affected or unaffected) (5) is obvious, and it is important to distinguish clearly between those seen and those not seen when the recording is made. Especially when close relatives are not seen, the reason should be stated, (6) for example, "died—1945—road accident" or "is in Canada" or "refuses co-operation" or "not traceable." Some doubt must always exist in certain conditions when a person is not seen.

The especial emphasis on recording the propositus or index case by which the family was first ascertained is made necessary because of reasons which are simple but would require too much explanation in these notes. For the same reasons, if the family was ascertained independently more than once, as, for example, if two

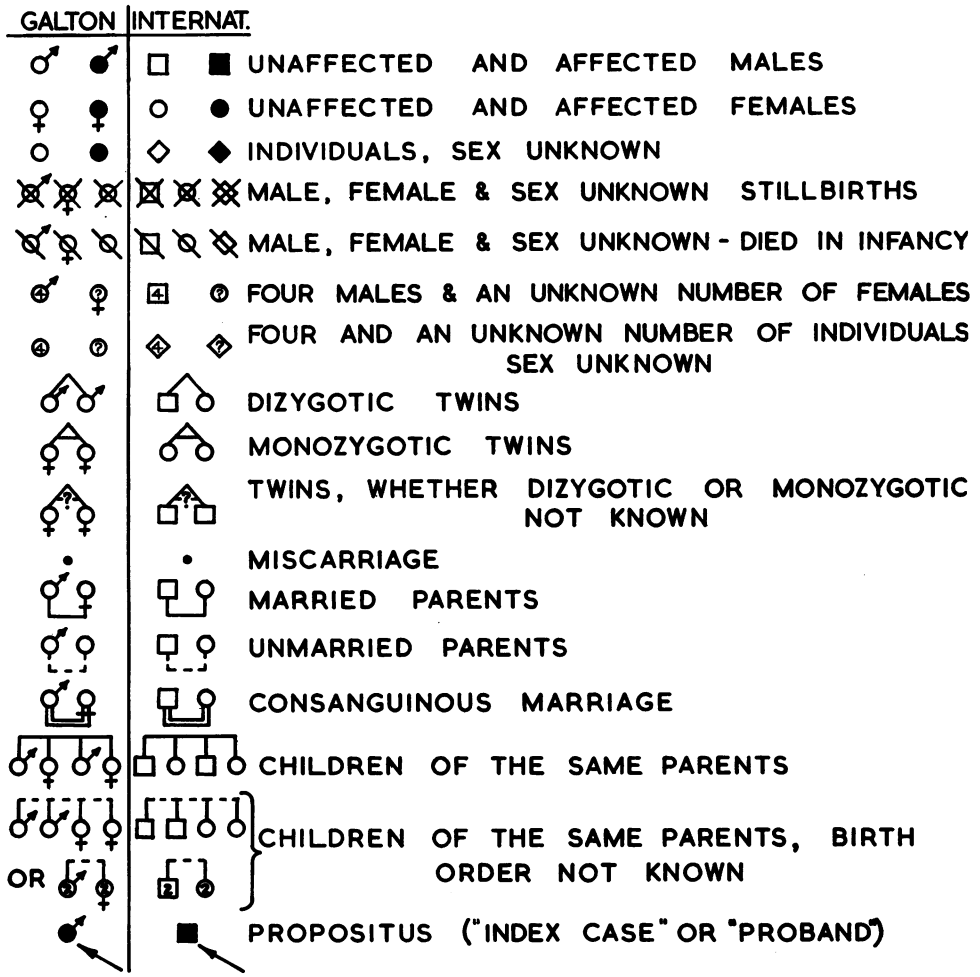
GALTON LABORATORY CONVENTION



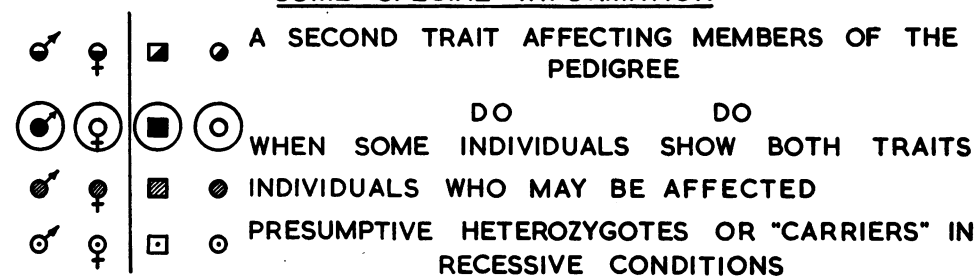
INTERNATIONAL CONVENTION



KEY TO PEDIGREE CONVENTIONS



EXAMPLES OF SYMBOLS WHICH MAY BE DEVISED TO SHOW SOME SPECIAL INFORMATION



affected sisters attended an out-patient clinic together, these facts should be reported.

Clearly all degrees of relationship to the propositus are not of equal importance when recording data. First in importance are the propositus and his or her brothers and sisters—collectively termed the sibship of the propositus. Next most important are the parents of the propositus and then their brothers and sisters (i.e., the uncles and aunts of the propositus). After that come grandparents, cousins, and other relatives.

The ages (preferably dates of birth) (4) of all relatives should be recorded in the priorities of the last paragraph, and if relevant, the ages of onset of all affected persons, including the propositus, should be given (8). This is of particular importance when the condition is not necessarily present at birth, but usually becomes recognisable only later. To take some obvious examples—the ages of sibs of children with rheumatic fever must be known if allowance is to be made for the fact that the condition is virtually unknown under three years of age, that there is a peak of incidence of first attacks between six and ten years and that probably over 30 per cent. of all persons who get rheumatic fever have their first attack over the age of 16 years. Again in Huntingdon's chorea the onset is commonly above the age of 30 years, and seldom, if ever, under the age of 20, so that sibs are at an ascending risk from zero to 40 years of age. Similar conditions apply to disseminated sclerosis. It will be clear from the foregoing that when a person is dead the age at death should be recorded.

Miscarriages and stillbirths need to be recorded as a routine when the information can be obtained. At times there is some question whether a gene usually expressed in the living subject determines intra-uterine death. Possibly also the homozygous state may be incompatible with life.

Linkage Data.

The amount of data available for study of linkage in man (i.e., parallel inheritance of two or more genes located on the same chromosome pair) is far behind the sophisticated mathematical methods which have been developed for their interpretation. With the ever-increasing recognition of blood groups determined by genes whose inheritance can be traced, opportunities for building up human chromosome maps became better every year, but there is a sad lack of information.

In every case of genetic interest, if at all possible the following specimens should be collected and tests made, especially from the sibship of the propositus and the parents.

(*a*) 5-10 cc. of whole blood (clotted specimen) for grouping with the request to the laboratory "complete genotyping for linkage purposes."

(*b*) 3-4 cc. of saliva collected in the morning before breakfast, free from toothpaste, phlegm, etc. It may be necessary to collect two mornings in succession to get sufficient. This should also be sent to a blood-typing laboratory for examination as to secretion in the saliva of AB group antigens.

(*c*) Colour vision should be tested by the Isehara method, and if there is any defect in the sibship the family should be referred for study.

(*d*) Ability to taste phenylthiocarbamide in 20 parts per 1,000,000 solution should be tested. In most cases persons can be classified clearly into tasters and non-tasters, but there will be some who are doubtful and some who at first say they do not taste but later have a delayed reaction of bitter taste in the mouth. Recordings should be made as "Taster," "Non-Taster," "Doubtful," and "Delayed Taster."

It is extremely important to record any abnormality or trait, other than the one under specific study, which is present in affected or unaffected members of the family. Such observations may give unique information about parallel inheritance of genes which may be of extreme rarity and yet, under certain circumstances, the opportunities may give valuable information on linkage. In other instances apparently unrelated traits may subsequently be proved to be the expression of the same gene.

As is well recognised, an undue proportion of persons whose trait is the expression of recessive genes, and who are homozygous for these genes, are the children of marriage of persons with a common ancestor. The rarer the gene the higher will be the proportion of affected persons who result from such consanguinous marriages. It is important therefore, in the first case, always to enquire carefully if there is any known relationship between parents of a person showing a specific trait. In reporting on the family there must be a definite statement "there was no known consanguinity" or "the parents were related in the following manner . . ." even if the relationship is clear from the diagrammatic pedigree.

The exact relationship must be specified. For example, in specimen pedigree I, given on page 56, the parents (V_1 and V_2) of the propositus (VI_1) were full cousins. V_1, the father of the propositus was the son of IV_1 who was a brother of IV_7 who was the mother of V_2, the mother of the propositus.

It is very important in the rare cases where the common ancestors are alive to get linkage data from them and successive generations.

The Setting out of Data.

The general relationship within the family or pedigree should be set out in diagrammatic form. The symbols used may be those of the so-called "international" system or those more commonly used in Britain—the conventions of the Galton Laboratory as used in the Annals of Eugenics. It is important if publication is contemplated to decide in advance the journal to which the paper is to be submitted and to use the convention adopted by that journal.

In referring to persons on the pedigree, reference must always be made in such a way that the symbol of the person can at once be identified on the pedigree. It is usual, once the pedigree has been drawn out, to number the generations vertically from above downwards in Roman numerals. Each generation is numbered from

left to right in Arabic numerals, so that III 9 would be the ninth person from the left in the third generation from the top of the pedigree.

In the two charts on pages 56 and 57 are set out the two conventions usually adopted for diagrammatic pedigrees.

The two conventions set out above are those used most commonly in all parts of the world. Different symbols, according to taste, are used to indicate information on pedigrees which is only required in a particular family. It might be, for example, that it was desired to differentiate between complete and incomplete expression of a gene as in Marphan's syndrome, where presence or absence of ectopia lentis could conveniently be shewn diagrammatically as well as in the text. Other examples are, when two traits are present in members of the same family so that there are two kinds of "affected" or when it was important either because they could be detected or because they could be presumed to indicate heterozygotes in a pedigree where the trait was expressed only in the homozygote.

A wide variety of symbols can be devised and a few examples are shewn below the specimen pedigrees. It should be remembered, however, that too many symbols are likely to defeat their purpose by making the pedigree laborious to interpret.

Finally, it should be remembered that a diagrammatic pedigree is merely a convenient picture and can never replace the more exact kind of information discussed in these notes which cannot be recorded graphically. An unexplained diagram. pedigree without notes on the diagnostic standards employed may be useless and misleading.

Streptomycin and the Tetracyclines in Acute Appendicitis

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THE use of penicillin and sulphonamide, intravenous fluid replacement and gastric suction greatly reduced the mortality and complication rates of acute appendicitis. For the past few years streptomycin, aureomycin, and terramycin have been available, and the purpose of this investigation was to determine whether or not their use had resulted in any further improvement in the mortality and complication rates.

MATERIAL.

I have traced 266 appendicectomies for acute appendicitis, performed by me in several hospitals in Northern Ireland, during the period November, 1947, to March, 1954. The degree of intensity of the inflammatory change present was judged by the naked eye, and recorded as the following stages :—

(1) Mild; (2) Acute; (3) Gangrenous; (4) Perforated; (5) Acute, gangrenous or perforated stages with pus locally; (6) Acute, gangrenous or perforated stages with general peritonitis.

As cases where, at operation, the inflammation is found to have spread beyond the appendix are most likely to be influenced by chemotherapy, only cases of stages 4, 5, and 6 have been included in this investigation. There were 58 in all, and of these 26 were treated with penicillin and sulphonamide, and 32 with either penicillin and streptomycin, aureomycin or terramycin.

The usual daily dose of penicillin was 400,000 units, sulphonamide 6 grammes, streptomycin 1-2 grammes, aureomycin 2 grammes, and terramycin 2 grammes.

RESULTS.

Table 1 gives the complications which occurred and their frequency. Table 2 gives the average number of days pyrexia, and average number of days in hospital after operation for each stage, with the different drugs used. Calculations were not made for any group which contained less than eight cases.

TABLE 1.

COMPLICATION.	PENICILLIN AND SULPHONAMIDE.	PENICILLIN AND STREPTOMYCIN.	AUREOMYCIN OR TERRAMYCIN.
Death	2	0	0
Paralytic ileus	2	0	0
Abscess	3	0	0
Abscess drained	2	0	0
Wound sinus	10	0	1
Fæcal fistula	1	0	0
Obstruction	1	0	0
Chest infection	4	0	0
Uræmia	1	0	0

TABLE 2.

Stage.	No. of Cases.	Days pyrexia.	S.D.	Days Hospital.	S.D.
Penicillin and Sulphonamide.					
5	8	4.4	4.3	19.1	3.5
6	17	9.9	10.6	31.3	20.5
Penicillin and Streptomycin.					
5	13	4.2	3.6	11.6	3.4
Aureomycin or Terramycin.					
6	12	7.5	5.4	14.6	4.5

Discussion.

Wakeley and Childs (1950) state that the Registrar General's figures for England and Wales show that the annual number of deaths from acute appendicitis has fallen from 3,178 in 1935 to 2,465 in 1939, and to 1,774 in 1945. Skyrme Rees (1950) states that it had fallen to 1,257 in 1948. In Northern Ireland the corresponding figures are 81 in 1939, 55 in 1945, and 18 in 1952. Gilmore and Lowdon (1952) found that the mortality for acute appendicitis in the Royal Infirmary of Edinburgh fell from 4.9 per cent. in 1930-1931 to 1.1 per cent. in 1948-50, and Skyrme Rees (1952) reports a fall of from 5.4 per cent. (1934-37) to 2.3 per cent. (1947-50). There has thus been a general fall in the number of deaths from acute appendicitis which could be due to such factors as earlier diagnosis, better operative technique, gastric suction, intravenous fluid replacement, as well as chemotherapy. However, as in this series under review all the cases were complicated by peritonitis, and gastric suction and intravenous fluid replacement were used where required, any improvement in the results must be due to the use of the newer, more powerful, drugs.

There were two deaths in the group of 26 cases treated with penicillin and sulphonamide, giving a mortality rate of 7.7 per cent., while there were no deaths in the 32 cases treated with the newer antibiotics. All other complications were reduced by the use of the newer antibiotics, and, in fact, only one complication developed, namely, one wound sinus.

Table 2 shows that, while streptomycin did not reduce the number of days of pyrexia in stage 5 cases, it did reduce the average number of days in hospital from 19.1 to 11.6. It is, however, in stage 6 cases that the greatest improvement has occurred. With the tetracyclines, the average number of days of pyrexia has been reduced from 9.9 to 7.5, and the average number of days in hospital from 31.3 to 14.6 (the difference between the means being 3.4 times the standard error).

Thus, the use of streptomycin or the tetracyclines in cases where the inflammatory changes have spread beyond the appendix has greatly reduced the mortality and complication rates, and there is also a marked reduction in the number of days in hospital after operation.

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Acute Porphyria

By R. J. KERNOHAN, M.D., M.R.C.P., D P.H., D C.H.

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PORPHYRIA is a rare disorder of metabolism, in which there is increased production and excretion of uroporphyrin, coproporphyrin, and porphobilinogen. Despite recent reviews (Goldman and Kaplan (1951), Watson (1951), and Janoff, Poutas, and Young (1953)), the disease is unfamiliar, but recently there have been an increasing number of case reports. Acute porphyria may present such varied symptoms that the diagnosis is often not considered for several years after the onset. In the following case the diagnosis was only considered when psychotic symptoms developed after laparotomy for an attack of undiagnosed abdominal pain. One sister of the patient has been treated in England for acute porphyria. Another sister, who died in 1946, had complained of symptoms which, in retrospect, are consistent with acute porphyria.

Case Report.—The patient was a young man, aged 21 years. He was admitted to hospital on 13th December, 1953. For twenty-four hours before admission he complained of crampy abdominal pain, and he vomited several times. During the previous year he had recurrent bouts of abdominal pain.

On examination, he was a well-nourished young adult. There was no abnormal pigmentation. The temperature was 100°F., and the pulse rate 100 per minute. The tongue was slightly furred and dry. He was tender over the right side of the abdomen, but there was no rigidity. A tentative diagnosis of acute appendicitis was made, and laparotomy was performed eight hours after admission. This revealed no evidence of disease of the abdominal visceræ. On the fifth post-operative day he had another severe attack of abdominal pain, and he vomited on six occasions. These symptoms were relieved by 50 mgm. pethidine.

After operation he had been persistently troublesome. On the eighth post-operative day he was found to be agitated, apprehensive, depressed, retarded, and introspective. He appeared to be preoccupied with religious ideas. He was very despondent and full of self-reproach. His attitude was peculiar in that he was kneeling in bed with his head over the edge, as if he were searching for something. There were many features of a catatonic schizophrenic episode. His mental state gradually improved, but three weeks later he was still mildly retarded and did not appreciate the possibility that his illness had been serious.

It was observed that the urine was red in colour, and the diagnosis of porphyria was entertained. It was found that there was a small, but abnormal amount of pre-formed porphyrin in the patient's urine, together with a large amount of the uroporphyrin precursor, porphobilinogen. On heating the urine at 100° C. for thirty minutes, especially if strongly acidified, the precursor broke down to give a greatly increased yield of uroporphyrin. The porphobilinogen was confirmed by the Ehrlich test (spectral band at 562) and the alkaline uroporphyrin was separated from the urine and showed a brilliant pink fluorescence in the ultra-violet, and four-band spectrum (at 610, 561, 540, and approximately 506). The blood serum showed no pink fluorescence. These results are consistent with a diagnosis of acute porphyria.

Family History.—A sister of the patient had been admitted to a mental hospital in County Antrim in 1947. She complained of weakness of her legs and general loss of energy. She also complained of severe pains in her legs and arms. She was pale and undernourished. Mentally, she was somewhat depressed, restless, and fretful. She did not sleep well. During the fortnight she was in hospital she had several slight rises of temperature, and the pulse was rapid from admission. Physical examination revealed little abnormal except a loss of power of the lower limbs. She died very suddenly. On the morning of her death she developed large blisters on the fingers and back of her hands.

Another sister has been treated in a London hospital for acute porphyria. She has complained intermittently of abdominal pain and depression. On admission to hospital, her blood pressure was 170/140. Her urine was found to be almost black, and contained 4,740 units porphobilinogen in a twenty-four-hour specimen.

The urines of all the other members of the family and twenty-five close relatives were examined for porphyrin pigments. None of these urines showed any Ehrlich test for porphobilinogen or any abnormal darkening on heating with or without acid.

There was no history of consanguineous marriages in the family.

Commentary.

It was reported in 1841 that the addition of strong sulphuric acid to hæmoglobin resulted in the precipitation of a red pigment. This pigment was given the name hæmatoporphyrin. Similar pigments were later isolated from the urine and fæces of normal people, but in larger amounts from urine of patients with a variety of diseases. Their characteristics were identified and named uroporphyrin and coproporphyrin. A precursor to these porphyrins, porphobilinogen, is pathognomonic of porphyria. In this the urine is frequently burgundy red in colour, and at times may show fluorescence. The name was changed from hæmatoporphyrin to porphyrin, and the disease is now called porphyria. The porphyrins are believed to be formed in the liver and are considered to be a by-product of hæmoglobin synthesis.

At one time porphyria was classified as congenital and acquired. It is now accepted that all forms are hereditary and that certain drugs, such as barbiturates, alcohol, sulphonal, trional, and heavy metals serve as precipitating factors. Clinically, three types are described.

1. *Photo-sensitive.*—This is more common in males, and may be pre-natal or shortly post-natal. The urine is deep red in colour. Garrod (1923) describes a case in which the very first urine passed by the child was red. The urine contains large amounts of uroporphyrin and coproporphyrin 1, both excreted in part as colourless, Ehrlich-negative chromogens. There is no Ehrlich-reacting porphobilinogen in the urine, and the absence of porphobilinogen is believed to have fundamental significance as regards the abdominal and nervous symptoms of acute porphyria. Blisters and bullæ develop on the exposed parts, resulting in scars. The occurrence of the cutaneous affection is dependent upon exposure to bright light. After repeated attacks, there is loss of substance and mutilation of the ears and nose. The nails may be shed from time to time, and atrophy of the terminal phalanges may occur. Formation of bullæ upon the conjunctivæ may result in blindness. The teeth are pink, due to pigmentation of the enamel. The bones show deep brown pigmentation,

which is due to deposition of porphyrin. Affected children may develop conspicuous hirsutes of the exposed parts.

2. *Mixed type.*—This is relatively uncommon. It has features of both the congenital and the acute type.

3. *Acute.*—This type is more common. The urine may be red upon voiding or become red on exposure to light. At times the urine is more icteric, and only after laboratory examination is the diagnosis of porphyria confirmed. Acute porphyria manifests itself with recurrent bouts of abdominal pain. Various neurological and psychiatric syndromes have been described, including paralyses, psychoses, and convulsions. Foot and wrist drop may occur, and not infrequently this proceeds to a symmetrical progressive ascending paralysis, with death from respiratory failure. Sensory disturbances are rare. The cardiovascular manifestations include tachycardia and T wave changes in the electrocardiogram. Hypertension, paroxysmal in type, is not uncommon in the acute attacks.

The symptoms in the acute cases are probably due to the action of the porphyrins on smooth muscle, causing spasm of the bowel and accompanying pain. Examination of the nervous system has sometimes revealed degeneration of nerve cells and myelin sheaths.

In the acute cases photosensitivity is usually absent. The demonstration of porphobilinogen is diagnostic of this type of porphyria. It is generally agreed that the development of neurological symptoms is of grave significance. The relation of the defect in porphyrin metabolism to the symptomatology and pathology is uncertain. Becker suggests that there may be interference with the synthesis and release of acetylcholine. It may be that porphobilinogen, present in acute porphyria with abdominal and nervous symptoms, but absent in congenital porphyria, may be responsible for the symptoms. The excretion of porphyrins may continue after the symptoms have subsided. Porphyrins in porphyria may have a rôle similar to uric acid in gout.

Porphyrinuria, usually an excess of coproporphyrins, must be distinguished from porphyria. The former may occur in a variety of conditions, including heavy metal intoxications, leukæmia, and liver disease. The diagnosis of porphyria depends upon presence in the urine of abnormal pigments such as porphobilinogen.

Treatment is unsatisfactory. Surgical procedures may precipitate a fatal attack. Watson recommends avoidance of such drugs as sulphonal, trional, and barbiturates. Liver extract and vitamins of the B group, especially riboflavin, folic acid, and vitamin B_{12}, have been widely recommended, but the results are questionable. Atropine and belladonna have been of no value. The possibility of adrenal dysfunction has been considered. In reported cases neither ACTH nor cortisone affected the clinical course of acute porphyria. Mellinger and Pearson (1953) describe one case in which a remission was produced by intravenous procaine hydrochloride, and consider that this is deserving of further trial. However, it is difficult to evaluate the efficiency of any treatment of acute porphyria on account of the tendency for exacerbation and remission, as well as by the relative rarity of

the disease. Treatment is directed primarily towards amelioration of the distressing symptoms, particularly pain.

Summary.

A case of acute porphyria is described. The diagnosis was made when psychotic symptoms developed after laparotomy for an attack of abdominal pain.

Two other members of the family have had symptoms of acute porphyria.

The diagnosis should be considered in cases of unexplained recurrent bouts of abdominal pain, neurological or psychotic episodes.

Treatment is unsatisfactory. Surgical procedures should be avoided. Certain drugs, especially the barbiturates, are contra-indicated.

We are very indebted to Professor D. C. Harrison, Queen's University of Belfast, for his report on the porphyrin pigments in the urine.

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REVIEWS

HISTOLOGY. By Arthur Worth Ham, M.B., F.R.S.C. Second edition. (Pp. xix + 866; figs. 518. £4.) London: Lippincott, 1953.

THIS is the most completely up-to-date text-book of histology available to-day. The book is complete and adequate for all but the most special study, but it avoids many of the details included in older and less selective text-books of histology. Instead, the author attempts to explain clearly the whole microscopic structures of the body and to evaluate the relative importance of what is described. He evidently has had great experience of the difficulties students encounter. Many experienced laboratory workers will find again and again clear expositions of the precise difficulties they themselves once experienced, and may well wish this book had been available to them sooner. Some parts of the book may seem too detailed, and perhaps the author might have indicated more clearly what a student might expect to see and recognise in such preparations as are likely to be available to him.

Unfortunately, this text-book is too detailed for most students in Great Britain. Good honours students and post-graduate workers will find it invaluable. In most British schools microscopic anatomy occupies much less of the students' time and effort than does gross anatomy. The shorter text-books used show little or no appreciation of those structural elements involved in disease. Books such as this show that modern histology is essential and basic in the study of medicine as a branch of biology. Function, normal and abnormal, should be studied in relation to structure. To those who think that medicine should be something more than a vocational training, and who believe the different subjects of the curriculum should not be studied in isolation from each other this book is recommended. It may stimulate a reassessment of the place of classical anatomy in the training of the student of to-day. J. E. M.

RESECTION-RECONSTRUCTION OF THE HIP. By Jean Judet, Robert Judet, Jean Lagrange, and Jean Dunoyer. Edited by K. I. Nissen. (Pp. xii + 151; figs. 99. 30s.) Edinburgh: E. & S. Livingstone, 1954.

IN the past few years an uncontrolled wave of enthusiasm for resection-reconstruction of the hip, using an acrylic prosthesis, in the treatment of various hip joint conditions, has swept the civilised world. It is extremely important, therefore, for all orthopædic surgeons to read carefully the experience of those who introduced the method. The Judet brothers, in their book, have analysed the results of their first four hundred cases and have indicated their experience with eight hundred and fifty cases in all. The book deals in detail with the technique employed and with the modifications necessary for the best results in different types of pathology. The authors have stressed the classes of patient which should be refused surgery. Throughout the book they emphasise the absolute importance of interfering as little as possible with the capsule of the hip, which they feel plays a very big part in the blood supply to the neck, and to what is left of the head, of the femur after the operation has been completed. The types of hip joint lesion which are amenable to the application of an acrylic prosthesis are osteo-arthritis, certain fractures of the neck of the femur, congenital dislocation of the hip in adults and a few other "odds and ends." The experience of the authors has been that 80 per cent. of patients gained excellent or satisfactory results, and this is of interest to the reviewer since the general experience of British orthopædic surgeons has not been anything like as good as this.

The book is well illustrated and the English is of a high standard. What the book unfortunately cannot tell the reader is the enthusiasm with which the authors have embarked on their project, nor can the book tell of the kindness and courtesy of the authors in their hospital and in their homes in Paris when they entertain, as they must be doing almost every week, visiting surgeons who have come to worship at the acrylic shrine of the Judets. R. J. W. W.

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A STUDY IN MANIC-DEPRESSIVE PSYCHOSIS; Clinical, Social, and Genetic Investigations. By Ake Stenstedt. (Pp. v+111. No price given.) Copenhagen: Munksgaard, 1952.

AMONG psychotic patients the manic-depressive has probably gained most from recent advances in treatment. In spite of this improving outlook, there has been a disappointingly small increase in our understanding of the nature of the disease itself. A real contribution to this understanding is made in this report of the epidemiology of manic-depressive psychosis in a Swedish county between 1919 and 1948.

All patients admitted to hospital with the diagnosis during the thirty-year period became the propositi, and their extended families yielded material for genetic and social study. There were 216 patients in the original sample (90 males and 126 females), and some 2,000 of their relatives were investigated. Among the relatives, 72 secondary cases were found, giving "morbidity risks" of 14 per cent. among siblings, 7.5 per cent. among parents, and 17 per cent. among the children of the propositi. The total morbidity risk for manic-depressive psychosis in Sweden is about 1 per cent. No important difference was demonstrated between the occurrence of other mental disorders in this group of relatives and the general population.

It is suggested tentatively that adverse environmental conditions in childhood might influence the emergence of psychosis among relatives of manic-depressives, and this is supported to some extent by the figures which are quoted.

The author agrees with other writers that the mode of inheritance of manic-depressive psychosis may be through a single autosomal dominant gene and cites thirty instances of successive generation attack from his study to support this He suggests that an "incomplete manifestation" of the disease may account for the discrepancy between the expected frequency among near relatives (50 per cent.) and that found in this and other studies (about 15 per cent.). Most British geneticists would probably be more conservative in their interpretation of this data and be inclined to think in terms of multiple gene inheritance. However, there is no doubt that the interaction of environment and the weight of inherited predisposition determines to some extent the "penetrance" or degree of expression of a clinical syndrome.

In 83 per cent. of the cases which were investigated the first attack was a depression, and it is encouraging to find that only half of all the manic-depressives in the study had more than one attack of the illness.

The report does not belittle the immense technical and methodological difficulties of a retrospective enquiry of this sort, and there is a full and useful description of the methods which were used.

E. M. B.

WATER, ELECTROLYTE AND ACID-BASE BALANCE. By H. F. Weisberg. (Pp. 250; 29 tables. 38s. 6d.) London: Ballière, Tindall & Cox, 1953.

THIS book is divided into three sections:—I, Normal Physiology; II, Pathological Physiology; III, Therapeutic Guideposts. Sections I and II are excellent. The descriptions of the processes involved in maintaining water and electrolyte balance are described sufficiently clearly to be understood by the non-expert; yet in sufficient detail to be useful to those working in the field. I do not know of any critical review on the subject which is as clear and comprehensive.

If there is a defect, it is that the account is not sufficiently speculative. I would like to have seen a discussion of the "Volume Receptor," hypothesis of Borst and Peters.

The third section on therapeutic guideposts is the shortest and the least satisfactory. The author states: "It is impossible to give a standard form of treatment to suit every patient; each must be evaluated separately." While this is true, I do believe that more definite guidance can be given in the matter of evaluation than is provided here.

Taken overall, I think this is the best available account of water, electrolyte, and acid-base balance that I have seen.

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THE ECZEMAS: A SYMPOSIUM BY TEN AUTHORS. Edited by L. J. A. Loewenthal, M.D., M.R.C.P., D.T.M. and H. (Pp. 267; figs. 77. 35s.) Edinburgh: E. & S. Livingstone, 1954.

THIS is a most interesting and at times exciting book which will be read and enjoyed by all those concerned in the management of eczema—but there are many faults. The editor has set himself an almost impossible task. He has attempted to unify the ideas on the subject of eczema as propounded with considerable vigour by nine authors (and himself), representing six different countries (England, Scotland, Switzerland, South Africa, United States of America, and Denmark). It is soon obvious to the reader that not only, as everyone knows, is there no international agreement on terminology, but there is little agreement on etiology or classification. Various editorial footnotes help to smooth out some of the rougher passages (for example, "The term 'allergic eczema' is to be taken as meaning 'allergic eczematous dermatitis' throughout this chapter: in chapter IV 'allergic eczema' is given as one of the synonyms of atopic dermatitis . . .").

To a professional dermatologist who, alas, has to have not only his own workable classification of the eczemas, but also a knowledge of the classifications employed by other authors, this defect is interesting and amusing, but it surely will be quite exasperating to others. But who was the book written for? In the last chapter we get a hint, ". . . a modicum of basic training has to be assumed." Why then are two pages devoted to a most elementary description of normal skin histology? Indeed, the whole chapter on histopathology is elementary and suitable for first hospital year students only. This contrasts strongly with the advanced experimental work described in detail in the subsequent chapter.

The reviewer was impressed by the forcefulness of the section on atopic dermatitis, but found the 1, 2, 3, 4, a, b, c, etc., method of presentation very difficult to read. Haxthausen's chapter on the theoretical considerations is fascinating and Bettley's chapter on contact eczema is full of practical advice. There is a little gem of summarising by Gordon on the involved subject of eczema of the hands, and the same author's differentiation of the types of eczema encountered in babies is noteworthy.

Throughout it all, the kindly pen of the editor fills in the gaps. The ". . . huge, hotly debated and uncertain problem" of nervous and emotional factors in the causation of eczema is presented in a way which appeals particularly to the reviewer when he writes: "Nevertheless, I believe that a psychosomatic explanation of ætiology, in the present state of our knowledge, must be subject to certain conditions: it should be the last factor considered, not the first; it should not be adduced simply through lack of a somatic explanation, that is by exclusion; and it should not be employed, in desperation, as an unconscious means of shifting the blame from our own inadequacy to the patient's temperament."

This book should certainly be studied by all qualified and potential dermatologists, and the very fact that it is written by people representative of six different countries offers a hope that soon international agreement on classification of the eczemas may be possible. If the ten dermatologists here could agree, maybe the rest of us would follow?

The book is well produced and bound. The type is clear, and there are few or no typographical errors. The illustrations are, for the most part, good. J. M. B.

HOSPITAL AT WORK. Published for the Middlesex Hospital. (Pp. 48; illustrations 150. 3s. 6d.) London: Max Parrish, 1954.

TO-DAY the public manifest an interest which is probably not entirely healthy in hospitals and operations, and especially in the more spectacular aspects of medicine. When so many sources pander to their appetite, it is well that a great hospital should present its work in a manner likely to interest the public, and at the same time with a minimum of emotionalism. This beautifully produced book is characterised by the highest technical excellence of photography, by editing as clever as that of the best illustrated papers and by commendable restraint. It should achieve its declared object of promoting the confidence of the patient in those who are looking after him. It should interest every doctor, and it is likely that his patients will be even more interested.

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Throughout it all, the kindly pen of the editor fills in the gaps. The ". . . huge, hotly debated and uncertain problem" of nervous and emotional factors in the causation of eczema is presented in a way which appeals particularly to the reviewer when he writes: "Nevertheless, I believe that a psychosomatic explanation of ætiology, in the present state of our knowledge, must be subject to certain conditions: it should be the last factor considered, not the first; it should not be adduced simply through lack of a somatic explanation, that is by exclusion; and it should not be employed, in desperation, as an unconscious means of shifting the blame from our own inadequacy to the patient's temperament."

This book should certainly be studied by all qualified and potential dermatologists, and the very fact that it is written by people representative of six different countries offers a hope that soon international agreement on classification of the eczemas may be possible. If the ten dermatologists here could agree, maybe the rest of us would follow?

The book is well produced and bound. The type is clear, and there are few or no typographical errors. The illustrations are, for the most part, good. J. M. B.

HOSPITAL AT WORK. Published for the Middlesex Hospital. (Pp. 48; illustrations 150. 3s. 6d.) London: Max Parrish, 1954.

TO-DAY the public manifest an interest which is probably not entirely healthy in hospitals and operations, and especially in the more spectacular aspects of medicine. When so many sources pander to their appetite, it is well that a great hospital should present its work in a manner likely to interest the public, and at the same time with a minimum of emotionalism. This beautifully produced book is characterised by the highest technical excellence of photography, by editing as clever as that of the best illustrated papers and by commendable restraint. It should achieve its declared object of promoting the confidence of the patient in those who are looking after him. It should interest every doctor, and it is likely that his patients will be even more interested.

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THIS is an unusual book and of a type which will be strange to British readers. It starts with a section in which are listed 1,585 symptoms and signs. Reference to any one of these directs the reader to some one of the 232 divisions of differential diagnosis, alphabetically arranged. These divisions describe the various causes of the symptoms, give diagnostic criteria and brief details of each clinical syndrome, including therapeutic tests and suggestions for treatment.

According to the author, the book has been prepared for office and bedside use by practising physicians for specialists retaining a broad interest in clinical medicine and for those undergraduates, interns, and residents who aspire to creative careers in private and institutional practice.

While the reviewer would not quarrel with its value for experienced practitioners, he does not consider that undergraduates or recently qualified doctors would find this a useful or helpful presentation of diagnosis in medicine. For the inexperienced, the detail is too brief to be successful, and such briefness may carry its own dangers.

Much of the book, however, will be of practical help to the experienced doctor. Many of the sections contain valuable suggestions and are well written, although in a brief, staccato style.

A long section of ninety pages on occupational hazards and their diagnostic features requires radical pruning, if the real dangers of industry are not to be buried in a welter of irrelevant details.

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The book is divided into three parts. Section I is devoted to a study of the embryology, anatomy, and physiology of the genito-urinary organs, Section II to the examination of the urological patient, and Section III to diseases of the genito-urinary organs.

The book is written for the senior student, and the young post-graduate. Each subject is dealt with in turn in an admirably clear and concise manner, and the text is greatly helped by the many beautiful drawings, photomicrographs, and X-ray pictures. These are of particular value in Section I.

In Section II, under methods of examination, the importance of the history and a detailed physical examination are stressed. The routine followed by the Harvard Medical School is given. More detailed examinations are then described, and the necessary precautions emphasised. Aortography is mentioned, but there is no reference to peri-renal insufflation.

In Section III a wide survey of the many urological diseases has been made, and the treatment adequately summarised. No details of the main operative procedures are given. Each is briefly mentioned.

This text-book is highly recommended to the senior student and the young doctor. It is a real pleasure to read. J. M. M.

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Only on one aspect can criticism be seriously offered, and that is, to the reviewer at least, the undue insistence on infection as the primary factor in stone formation.

Inevitably purely bio-chemical work is only referred to in a limited way, although it seems likely to provide the most hopeful approach to prevention. A section on this approach by a worker in this field would be of great value in future editions. C. J. A. W.

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Inevitably purely bio-chemical work is only referred to in a limited way, although it seems likely to provide the most hopeful approach to prevention. A section on this approach by a worker in this field would be of great value in future editions. C. J. A. W.

SPOT DIAGNOSIS. By the Editors of "Medicine Illustrated." (Pp. 128; figs. 102. 7s. 6d.) London: Harvey & Blythe, 1954.

In this little book the editors of "Medicine Illustrated" have collected clinical photographs of over one hundred cases that have appeared in that journal. Each is presented as a problem in diagnosis, with the answer and a short description of the condition and its treatment on the following page. The majority of cases illustrated are common surgical and dermatological conditions, but the scope extends as far as air encephalography and the histology of uterine scrapings. At the end of the book there are useful notes on modern therapeutics in such conditions as peptic ulcer, thyrotoxicosis rheumatoid arthritis and tuberculosis.

The book is clearly intended primarily as an aid to revision for the final year student, and should prove useful and refreshing for this purpose. It should also be of interest and value to post-graduates and general practitioners. Nearly all the reproductions are of a very high quality, though a few of the X-rays are indifferent.

It will be interesting to see how the student reacts to this educational experiment, but it is to be hoped that he will not attempt to use it as a substitute for live clinical cases. It is not possible, for your reviewer at least, to diagnose such conditions as sebaceous cyst and cold abscess without using the sense of touch. In spite of its limitations, this book is strongly recommended to the student, particularly in his final year. T. K.

ESSENTIAL UROLOGY. By F. H. Colby, M.D. Second edition. (Pp. x + 650; illustrations 352. 61s. 6d.) London: Ballière, Tindall & Cox, 1953.

The second edition of this book, the first edition of which appeared in 1950, is an account of the science of urology as practised at the Massachusetts General Hospital.

The book is divided into three parts. Section I is devoted to a study of the embryology, anatomy, and physiology of the genito-urinary organs, Section II to the examination of the urological patient, and Section III to diseases of the genito-urinary organs.

The book is written for the senior student, and the young post-graduate. Each subject is dealt with in turn in an admirably clear and concise manner, and the text is greatly helped by the many beautiful drawings, photomicrographs, and X-ray pictures. These are of particular value in Section I.

In Section II, under methods of examination, the importance of the history and a detailed physical examination are stressed. The routine followed by the Harvard Medical School is given. More detailed examinations are then described, and the necessary precautions emphasised. Aortography is mentioned, but there is no reference to peri-renal insufflation.

In Section III a wide survey of the many urological diseases has been made, and the treatment adequately summarised. No details of the main operative procedures are given. Each is briefly mentioned.

This text-book is highly recommended to the senior student and the young doctor. It is a real pleasure to read. J. M. M.

STONE IN THE URINARY TRACT. By H. P. Winsbury-White. Second edition. (Pp. ix + 328 + xiv; figs. 144. £3. 3s.) London: Butterworth, 1954.

A volume of this size and price, devoted to a limited but important aspect of urinary tract lesions, will naturally appeal mainly to those whose interest lies chiefly in urological diseases.

The subject is comprehensively dealt with by a surgeon of high repute and wide experience in this field, and will be an invaluable reference work to all who encounter these conditions.

Only on one aspect can criticism be seriously offered, and that is, to the reviewer at least, the undue insistence on infection as the primary factor in stone formation.

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