Factors which may precipitate auricular fibrillation include exercise, emotion, infection, and active carditis, but usually no cause is apparent.

The onset of auricular fibrillation may pass unnoticed or be responsible for dyspnoea, pulmonary oedema, pulmonary infarction, systemic embolism, cardiac failure, loss of consciousness, or anxiety.

Relative advantages of established auricular fibrillation include freedom from paroxysmal attacks, ease of control of heart rate with digitalis, and comparative freedom from bacterial endocarditis.

Persons with auricular fibrillation tend to have larger hearts than those in sinus rhythm, but reasons are given for concluding that enlargement is not directly related to the arrhythmia.

Possible factors in the pathogenesis of auricular fibrillation are reviewed, and it is concluded that there is presumptive evidence that myocardial damage may be the most important.

Auricular fibrillation is not a contraindication to valvulotomy but a disadvantage from the presumed presence of myocardial damage and the increased probability of clot being present, with the consequent risk of embolism.

Auricular fibrillation had occurred pre-operatively in 42% of the surgical series. In these 106 patients clot was found in the left auricle or atrium in 40%, but in only 3 of 144 patients in sinus rhythm.

The presence of a regurgitant jet seems to militate against thrombus formation.

Good operative results may be obtained in cases of auricular fibrillation and life thereby prolonged, but the operative risk is greater and the ultimate prognosis poorer than in cases with sinus rhythm.

Post-operative auricular fibrillation occurred in 23% of those previously in sinus rhythm. In the first 10 post-operative days it is rarely possible to restore sinus rhythm with quinidine, but thereafter success is almost always obtained. Pre-operative prophylactic quinidine is ineffective.

REFERENCES

- Blumgart, H. L. (1924). *Heart*, 11, 49.
 Comeau, W. J. (1942). *New Engl. J. Med.*, 227, 134.
 Degraft, A. C., and Lingg, C. (1935). *Amer. Heart J.*, 10, 630.
 Fraser, H. R. L., and Turner, R. W. D. (1955). *Brit. Heart J.*, 17, 459.
 Harrison, C. V., and Wood, P. (1949). *Ibid.*, 11, 205.
 Hay, J., and Jones, H. W. (1927). *British Medical Journal*, 1, 559.
 Mackenzie, J. (1911). *Heart*, 2, 273.
 Stroud, W. D., Laplace, L. B., and Reisinger, J. A. (1932). *Amer. J. med. Sci.*, 183, 48.

Among organizations which help to maintain friendly international relations on the medical plane, the Horse Shoe Club is particularly concerned with fostering friendship between American, Canadian, and English men and women interested in the cure and prevention of disease. The club encourages exchange research and clinical appointments between these countries, and provides hospitality for overseas visitors. On November 12, at Apothecaries' Hall, the Horse Shoe Club held its autumn cocktail party (one of two held every year) to entertain doctors from the U.S.A. and Canada who are working here for the time being either in their country's armed Forces or in civilian posts, together with their wives. Dr. GEOFFREY BOURNE, chairman of the club, Sir HARRY HAGUE, treasurer, and Dr. CLAUDE NICOL, secretary, were all present. Many of the 150 guests took the opportunity of hearing Dr. NEVILLE FINZI, master of the Society of Apothecaries, discourse on some of the treasures of the Society.

ACTINOMYCIN C IN TREATMENT OF ADVANCED HODGKIN'S DISEASE

BY

J. R. TROUNCE, M.D., M.R.C.P.

A. B. WAYTE, M.B., D.M.R.E.

AND

J. M. ROBSON, M.D., D.Sc., F.R.S.Ed.

*From the Departments of Medicine, Radiotherapy,
and Pharmacology, Guy's Hospital*

In 1949 Brockman and Grubhofer isolated from *Streptomyces chrysomallis* a substance which they named actinomycin C ("sanamycin"). Three years later, Hackmann (1952) reported that this substance had an inhibiting effect on the growth of the Ehrlich carcinoma, a mouse sarcoma, and the Walker carcinoma in rats. He also noted that actinomycin C had a cytostatic effect, particularly on the lymphatic system (Hackmann, 1953).

As a result of these findings, Schulte (1952) treated a number of patients with tumours of the reticulo-endothelial system with this substance and reported some improvement in their condition, with disappearance of the tumours in some cases and in others a reduction of the dose of radiation required to control.

A large series of patients was investigated by a group of French workers (*Presse méd.*, 1954). It was stated that the effect of actinomycin C in Hodgkin's disease was inconstant and of short duration. Two of the group, however (Ravina and Pestel, 1954), reported considerable improvement in Hodgkin's disease. Their better results may have been due to the large dosage of actinomycin C, which was given in gradually increasing doses up to 1,200 μ g. a day. Each daily dose was given by intravenous drip spread over three to four hours.

The toxic effects were confined to the gastro-intestinal tract, and consisted of stomatitis, pharyngitis, nausea, and diarrhoea. Actinomycin C was also tried in acute leukaemia and various carcinomas without effect.

Present Investigation

Actinomycin C was given to six patients with Hodgkin's disease and one with a reticulum-celled sarcoma. All the patients had already been treated by radiotherapy, and all but one had received one or more courses of nitrogen mustard; these courses, however, were not completed in two cases owing to toxic effects. All the patients were suffering from an advanced stage of the disease.

Dosage.—The usual scheme of dosage employed was to start with 100 μ g. of actinomycin C intravenously. If no toxic effects were observed the dose was increased so that at the end of a week or ten days the patient was receiving a daily dose of 400 μ g. The dose was then progressively increased to 600 μ g., and finally 800 μ g. a day. With doses of 400 μ g. or more the drug was dissolved in half a pint (285 ml.) of saline, and given by intravenous drip over about two to three hours. A total course of between 7,000 and 10,000 μ g. was used whenever possible. In one patient who responded to the drug but relapsed rapidly an attempt was made to maintain improvement with twice-weekly injections of 400 μ g. This was carried out for two months, but did not appear to be effective.

Results

The results of treatment are summarized in Table I. Only two patients showed a marked response to treatment, with disappearance of fever and considerable reduction in the

TABLE I.—*Results of Treatment*

Case No.	Diagnosis	Total Dose of Actinomycin C	Therapeutic Effect	Toxic Effects	Follow-up	
					Period	Results
1	Hodgkin's disease	4,600 µg.	None	None	—	Died during treatment
2	" "	4 courses (5,000 µg., 8,000 µg., 5,000 µg., and 4,000 µg.) (biweekly doses)	Slight	Stomatitis; thrombocytopenia; pigmentation	6 months	Died
3	" "	5,400 µg.	"	Hair loss; stomatitis; thrombocytopenia; rash; leucopenia	8 "	Some improvement maintained
4	" "	9,100 "	None	None	6 "	Further deep x-ray required
5	Reticulum-celled sarcoma	7,000 "	Marked	"	3 "	Marked improvement maintained
6	Hodgkin's disease	4,500 "	None	Stomatitis; pigmentation	—	Died during treatment
7	" "	7,500 "	Marked	Rash	3 weeks	—

size of lymph nodes and spleen. In one of these patients improvement has been maintained up to the present, a period of three months. Two other patients showed slight improvement, with some reduction in the size of lymphatic glands and temporary disappearance of fever. Three cases showed no response to the drug; but two of these patients died of their disease before completing the course of treatment, and therefore did not really afford an adequate trial for the drug. Where improvement occurred it was slow, and reduction of fever appeared only after a week or more.

Toxic Effects.—(a) *Thrombocytopenia*: The most serious side-effect noticed was thrombocytopenia. This occurred in two patients; the details are summarized in Table II. In Case 2 a retroperitoneal haemorrhage required laparotomy

TABLE II.—*Cases in Which Thrombocytopenia Occurred*

Case No.	Platelet Count before Treatment	Total Dose of Actinomycin C	Lowest Platelet Count	Platelet Count after 1 Week on Cortisone
2	200,000	5,000 + 8,000 µg.	10,000	30,000 (80,000 after 1 month)
3	130,000	5,400 µg.	42,000	100,000

and transfusion. In both patients the actinomycin C was stopped, and they appeared to respond to cortisone, 150 mg. daily; and in Case 2 further administration of actinomycin C combined with cortisone did not lead to a recurrence. Although thrombocytopenia may occur during the course of Hodgkin's disease (Gledhill and Shillitoe, 1952), it seems very much more likely that in these two patients it was associated with the actinomycin C—suggesting that, if the drug is given, a careful check should be kept on the platelets. (b) *Other Side-Effects*: The other side-effects noticed were sore mouth (three patients), erythematous rash (two patients), brown pigmentation of the skin (two patients), slight loss of hair (one patient), and moderate leucopenia (one patient).

Discussion

The results in this small series suggest that, in advanced reticulososes, actinomycin C only occasionally has any great effect on the disease. Its place in the treatment of this group of conditions is difficult to assess at present, but it would seem to be worthy of a trial when the other more usual treatments have failed, and particularly in those patients who for one reason or another are unable to take nitrogen mustard.

The other possible use for the drug might be in combination with either deep x rays or nitrogen mustard in an attempt not only to increase the therapeutic effect but perhaps to prevent the appearance of resistance to further treatment at a later date in those patients who respond satisfactorily, or to increase the sensitivity to radiation of those cases that have become radio-resistant.

Summary

Six cases of Hodgkin's disease and one of reticulum-celled sarcoma have been treated with actinomycin C.

In two patients there was marked regression of the disease, and in two slight regression.

The side-effects of the drug included stomatitis and thrombocytopenia. The importance of repeated examination of the blood during treatment is stressed.

We would like to thank Dr. D. I. Finer, the family doctor of one of the patients, for his co-operation, and Dr. Wilpert, of Farbenfabriken Bayer, for the supplies of sanamycin.

REFERENCES

- Brockman, H., and Grubhofer, N. (1949). *Naturwissenschaften*, 36, 376.
 Gledhill, R. C., and Shillitoe, A. J. (1952). *British Medical Journal*, 1, 1336.
 Hackmann, C. (1952). *Z. Krebsforsch.*, 58, 607.
 — (1953). *Strahlentherapie*, 90, 296.
Presse méd., 1954, 62, 737-44.
 Ravina, A., and Pestel, M. (1954). *Presse méd.*, 62, 743.
 Schulte, G. (1952). *Z. Krebsforsch.*, 58, 500.

ALBUMINURIA IN SERVICE RECRUITS

BY

F. S. FOWWEATHER, M.D., M.Sc., F.R.C.P.

(From the Department of Chemical Pathology,
University of Leeds)

The time is long past when albuminuria was regarded as synonymous with renal disease; benign albuminuria is a well-recognized condition. When albuminuria is found in a recruit who, apart from this, appears to be quite fit for service, the possibility of the albuminuria being benign calls for consideration, and before reaching a decision on this point the chairman of the medical board concerned may refer the recruit for examination by a pathologist. In addition to albuminuria there may be features in the past history of the apparently healthy recruit—"kidney disease," scarlet fever, etc.—which suggest the possibility of a legacy of latent nephritis, and so reinforce the advisability for as full an examination as possible before a final decision is reached concerning the suitability of the recruit for service. The same considerations of course arise with respect to examinations for insurance, and sometimes for employment. I have been dealing with cases referred for pathological examination since 1940. The examinations were planned at short notice, to give the medical boards the information asked for, with no thought of publication at the time, but I believe the results obtained to be of sufficient interest to be placed on record.

Method

Recruits for examination are instructed to have only a light breakfast, with not more than one cup of weak tea (coffee is forbidden), and they are asked to present themselves at 10 a.m. On arrival they are immediately instructed to empty the bladder, and the urine is kept for examination.