MEDICAL PRACTICE

Occasional Survey

Ten-year Survey of Treatment with Implanted Cardiac Pacemaker

E. SOWTON, G. HENDRIX, P. ROY

British Medical Journal, 1974, 3, 155-160

Since the first implant of an artificial cardiac pacemaker in a patient by Senning in 1958 the reliability of apparatus has increased considerably and the indications for long-term pacing have greatly extended. In this paper we present the clinical results obtained in 372 patients attending the pacing clinic at Guy's Hospital up to 31 December 1973. Particular reference is made to the changes in indications in recent years and to the reliability of present apparatus.

Patients

There were 239 (64%) males and 133 (36%) females, with ages ranging from 12 to 90 years, (mean 66 years) at the time of pacemaker implantation. Forty one per cent of the patients were aged 70-79 years. The sex distribution was very similar in all age groups.

Aetiology

Thirty-two patients (8.6%) had associated ischaemic heart disease as judged by cardiac infarction, angina, or E.C.G. evidence before the onset of heart block though this was not proved to be the cause of the block. Thirty patients (8%) probably had high block in the atrioventricular node, diagnosed on the basis of a narrow QRS complex, a rapid ventricular rate which in-

creased with effort, and a normal sized heart on x-ray examination. It is impossible to determine how many of these had congenital block because the age at presentation varied from 12-52 years. There were 24 patients (6.5%) in whom the block was attributed to miscellaneous causes such as calcific aortic stenosis, myocarditis, Chagas's disease, Reiter's syndrome, or cardiomyopathy. The remaining 77% were diagnosed as having degenerative fibrosis of the conducting system. These aetiological factors applied about equally to both sexes except that 23 of the 32 patients with ischaemic heart disease were male.

Indications for Pacing

Pacemakers were implanted because of syncopal episodes in 290 patients (78%) and because of dizziness or near-syncope in a further 30 (8%). Thus 86% were paced for a Stokes-Adams attack, either major or minor. Twenty-four patients were paced because of heart failure and bradycardia without syncope, three because complete heart block persisted one month after cardiac infarction, and two because they needed long-term pacing after cardiac surgery.

Twenty patients were paced because of intermittent episodes of supraventricular tachycardia (flutter, fibrillation, paroxysmal atrial tachycardia, etc.) alternating with severe bradycardia. Various supraventricular natural pacemakers arose and junctional rhythms were common. Other patients who were paced for tachycardia alone are being reported separately and were not included in the present report.

Of the patients with syncopal episodes 16 also had heart failure. Of a total of 40 patients with heart failure 18 had ischaemic heart disease. All the patients with narrow QRS complexes were paced because of syncope.

It proved impossible to determine the time of onset of heart block in most patients, but the delay between the first Stokes-Adams attack and the start of pacing in 309 patients ranged from 13 years to one day (mean 18 months). In 18 patients

Cardiac Department, Guy's Hospital, London SE1 9RT

E. SOWTON, M.D., F.R.C.P., Consultant Cardiologist

G. HENDRIX, M.D., Associate Professor of Medicine, University of South Carolina, Present address: Department of Cardiology, Medical University of South Carolina, Charleston, South Carolina 29401, U.S.A.)

P. ROY, M.R.C.P., Research Fellow

asymptomatic heart block had been documented from three months to 10 years (mean 36 months) before the onset of syncope. The mean time of symptoms (syncope) in patients with narrow QRS complexes was six months.

Type of Heart Block

Complete 12-lead electrocardiograms were obtained before the onset of pacing in 191 patients. In the remainder no record could be obtained, either because temporary pacing had already been started elsewhere or because a transvenous electrode had to be introduced urgently to prevent syncopal attacks. In a further 35 cases sufficient data were available to determine whether the block was stable or intermittent. In these 226 cases complete heart block was twice as likely to be stable as partial block.

In the 191 patients with full pre-pacing E.C.G.s the presence or absence of bundle-branch block and the mean QRS axis (frontal plane) were analysed. An axis of $+89^\circ$ to $+29^\circ$ was accepted as normal and 75 patients (39% of the 191) fell into this group. Of these patients 39% had normal QRS complexes, 31% had right bundle-branch block (R.B.B.B.) pattern, and 19% had left bundle-branch block (L.B.B.B.). All patients with axes beyond -44° or $+119^\circ$ also had bundle-branch block.

Of the 146 patients with bundle-branch block (76% of the 191), 102 had R.B.B.B. pattern and of these 51 (50% of the 102) had left axis deviation; 22 patients had a normal axis. Of the 44 cases with L.B.B.B. pattern 27 (61% of the 44) had left axis, one had right axis ($+120^\circ$), and the remaining 16 (36%) had a normal axis.

The finding that three-quarters of our patients had wide QRS complexes is consistent with the concept that chronic heart block is due to peripheral disease in the fascicles of the conducting system rather than to proximal disease in the atrio-ventricular node.^{1 2} There was no correlation between the type of block (partial or complete, stable or intermittent), the axis, and the presence of wide QRS complexes.

In 23 patients E.C.G.s taken before the onset of any degree of heart block were available. Seven of these showed evidence of conduction disturbance in two of the three fascicles; in these patients heart block developed after a mean period of 36 months (range eight months to six years). Thirteen patients had evidence of delay in one fascicle only, and they developed heart block after a mean time of 41 months (range seven months to 11 years). In three patients the E.C.G.s were normal and heart block developed after one month, 12 months, and seven years.

The P-R interval could be obtained from E.C.G.s showing conducted beats before pacing in 50 patients. The interval exceeded 0.21 sec. in 18 (36% of the 50) but there was no relation between the P-R interval (which ranged from 0.10 sec. to 0.44 sec.) and the axis, stable or intermittent block, or widening of the QRS complex.

Idioventricular Rate

The prepacing rate was available in 150 patients; the slowest rate was 7 beats/min, and three patients receiving sympathomimetic drugs had rates of over 70 beats/min. There was no correlation between rate and type of block, axis, atrial rate, or type of QRS complex. The mean idioventricular rates were not faster for patients with narrow QRS complexes.³

Pacing Technique

The early patients in this series were treated with epicardial electrodes, but it is now our standard practice to use the transvenous approach as the method of choice. Overall 336 patients (90%) had transvenous systems initially. Epicardial electrodes were used when it proved impossible to obtain a stable position for a transvenous electrode or when a thoracotomy was indicated

for cardiac surgery. During the 10 years covered by this survey 15 of the 372 (4%) patients were changed from transvenous to epicardial and another nine (2.4%) from epicardial to transvenous.

The choice of vein has changed considerably during the time of this study, most implants being performed via an external jugular vein until 1971. During 1972 72% and during 1973 over 90% of transvenous electrodes were inserted via a cephalic vein. Right sided veins were used about twice as often as left sided ones.

Over 95% of all transvenous implantations and generator replacements are now carried out under local anaesthesia (with 1% lignocaine). The patient is premedicated with diazepam and is also given diazepam intravenously at the start and as needed during the procedure. The total intravenous dose is usually 10-20 mg. Many patients fall asleep during the procedure, but in a few cases additional pethidine or diamorphine must be given. The use of local anaesthesia has greatly reduced delays before implantation and has eliminated postoperative respiratory complications. Antibiotic solution is left in the pacemaker pocket and a 5-day course of oral antibiotics is given post-operatively.

Type of Pulse Generator

Both ventricular inhibited ("demand") and ventricular-triggered pacemakers have been used with increasing frequency since their introduction in 1966, so most initial systems were of this type from January 1971 to 31 December 1973, compared with only 46% in 1967-8. Overall 242 (65%) of the 372 patients were initially given demand pacemakers and 123 (53%) of 233 replacement pacemakers were also of this type. During the last two years we used ventricular-inhibited demand pacemakers to the virtual exclusion of ventricular-triggered models.

Our present policy is to implant a demand pacemaker in patients who have intermittent atrioventricular conduction or frequent ectopic beats during temporary pacing. Fixed-rate units are chosen for patients with stable complete heart block; if atrioventricular conduction subsequently returns the fixed-rate pacemaker is not normally removed, but a demand pacemaker is substituted when the batteries are exhausted. The risk of pacemaker-induced ventricular fibrillation due to stimulation on the T wave of spontaneous beats seems to be small with modern pacemakers and electrodes once the initial trauma of electrode placement has passed. Demand pacemakers are used to avoid unpleasant palpitations due to competition and to allow haemodynamically superior sinus beats to occur unimpeded as often as possible. Atrial-triggered pacemakers have been used only in a few young patients, largely because this installation still requires thoracotomy for satisfactory attachment of the atrial sensing electrode. In only one patient have we achieved long term transvenous atrial pacing (for three years so far).

Eight different types of fixed-rate pacemakers and 20 types of demand or standby pacemakers have been used, but we now use the Devices 2970 for fixed rate pacing and Devices 3821 for demand pacing. During 1 May to 31 December 1972 56% of 10 pacemakers used were demand and 44% were fixed-rate. Between 1 January 1973 and 31 December 1973 78% of 202 pacemakers used were demand models.

Unipolar and bipolar electrodes have been used as provided by the manufacturers, with no major differences in performance, but because of our follow-up method of impulse analysis we prefer unipolar systems, since the pacemaker impulse deflection on the E.C.G. is far larger than with bipolar electrodes.

Time in Hospital

The average stay in hospital for patients having initial implants during 1962-4 was 55 days, and during 1967-8 it was 25 days. During 1971-2 most patients having initial implants were in

hospital for 10 days or less. This time was largely determined by the time needed before stitches were removed (seven days), and in some cases patients were able to return home a few days after implantation and have the stitches removed by their general practitioner or in a local hospital. We now close all pacemaker incisions with subcuticular absorbable sutures (Dexon) so that no stitches need removing, and this has further shortened the hospital stay. During 1973 most patients having initial implants were in hospital for less than one week.

Threshold Measurements

The initial threshold was measured at implantation using a standard technique in all except the very early cases. A Devices adjustable pacemaker, providing a 2 msec stimulus, is attached to the electrode and good subcutaneous contact in the incision is made with a clamp to provide a positive indifferent electrode. The heart is paced at 70/min (or at 5-10 beats above the spontaneous rate if sinus rhythm is present) using a 3-volt stimulus. The amplitude is then reduced slowly until failure of pacing occurs, at which point the threshold is read from the pacemaker calibration. The mean initial threshold for 365 patients was 0.54 volts, with a range of 0.1 to 2.6 volts. We now consider an initial threshold of greater than 0.8 volts unacceptable, and repeated attempts are made to reposition the electrode until a level of less than 0.6 volts is obtained. The threshold measurement is repeated several times as the implantation proceeds to ensure that the value remains low. In 20 patients Elema-Schönander Vario pacemakers were used, allowing repeated threshold measurements to be made during and after the procedure as well as at follow-up visits. The threshold results in these patients did not differ from the whole group.⁴

A total of 106 patients had thresholds measured with the same technique when generators were replaced, giving a mean value of 1.7 volts. We now consider a late threshold (as measured with Devices, Cordis, Medtronic, or Elema transvenous wires) of over 3 volts is unacceptable and introduce a new electrode or, in a few cases, a high output pacemaker. There was no apparent relation in individual cases between the initial and late thresholds.

Complications

HIGH THRESHOLD

Early failure of pacing due to an increase in threshold above the output of the pacemaker (exit block) occurred in 22 cases (6%). Minor changes in electrode position, not detectable on x-ray examination, might have accounted for some of these cases. The initial thresholds in these patients averaged 0.57 volts and only one patient had an initial level above 1.1 volts. This group, therefore, was not significantly different in this respect from that without this complication. The mean threshold at operation for repositioning the electrode in 18 patients was 5.9 volts (range 3.2 volts-9.0 volts). The other four patients were successfully treated with a course of prednisone (40 mg/day for one week), and pacing was re-established without operation. Steroid therapy failed in two cases and the electrodes were repositioned. Two further pacemakers failed to sense spontaneous beats but continued to pace satisfactorily as fixed-rate units. Fourteen other patients were classified as having a failure of pacing due to late high threshold because at reoperation the threshold level was found to exceed 3 volts, but in this group the situation became apparent only because of depletion of a battery.

ELECTRODE MOVEMENT

In the last 100 patients early failure of pacing occurred in eight owing to known movement of the electrode tip. The average initial threshold in these eight patients was 0.54 volts. Reposi-

tioning of the electrode was sufficient in six of these patients. In two patients movement of the electrode tip occurred, necessitating insertion of an epicardial pacing system. In a few cases we were able to show a new electrode position was satisfactory by non-invasive threshold measurements using the Elema Vario system.

INFECTION AND SKIN NECROSIS

It is usually impossible to distinguish between a sterile reaction and a low-grade infection, particularly since actual breakdown of skin is invariably accompanied by obvious infection. Twenty-five patients (7%) had an early reaction around the pacemaker with excessive fluid formation, but cultures of aspiration samples were sterile. In eight of these cases there was skin tension leading to necrosis, either actual or potential, sufficient to require re-siting of the unit. This complication did not occur during the last year. Positive cultures from infected pacemakers were obtained in 28 cases over the 10 year period, almost invariably in patients with late breakdown of skin covering the pacemaker after several months of pacing. We now aspirate excess fluid in the rare cases when this accumulates after pacemaker implantation using a small needle and approaching from above through normal skin. The fluid is sent for culture and gentamicin 80 mg together with 10 mg prednisone is left in the pacemaker pocket.

In the whole series over the 10-year period 10% of patients had to undergo removal of the pacing system because of local reaction or infection and with reimplantation of a new electrode and generator in a different site. In 10 patients with low grade infection or sterile reaction associated with painful and tense swelling of the pacemaker pocket antibiotic treatment was completely successful. In three other patients with frank infection and discharge through the skin antibiotics were also successful. In all cases direct injection into the pocket together with large doses by mouth were used.

Results of Pacing

MORTALITY

There were no deaths associated with the initial pacemaker implantation, nor with subsequent generator replacements. Of the 372 patients 31 died between one month and six years after the initial implantation. The mean age at death of these patients was 73 years (48-88). The cause of death was carcinoma in two cases and unknown in the remainder. We know of no death from pacemaker failure or electrode movement. The yearly mortality is at present about 7.5% for patients with ischaemic heart disease and about 2.5% for those without.³

CONTROL OF SYMPTOMS

Stokes-Adams attacks were extremely rare after discharge from hospital and could always be traced to a pacing fault. One patient had an attack because of early exit block and two because of transvenous electrode displacement; all three were subsequently free from attacks when the complications had been treated. The 78% of patients in whom this symptom formed the indication for pacing were thus completely relieved, and the additional 8% with syncope and heart failure were freed from their attacks, of unconsciousness.

The effect of pacing on heart failure cannot be reliably assessed because antifailure drugs were also used whenever indicated. About half our patients received digoxin and diuretics in addition to pacing and this therapy was used more freely than before pacemaker implantation. This was in part due to the frequent clinical assessment implicit in our pacemaker follow-up system, but it also probably reflects a general reluctance to use digitalis in unpaced patients with slow ventricular rates.

Slightly more than 60% of all patients were judged clinically to have improved in this respect at their one month follow-up visit.

CONTROL OF TACHYCARDIA/BRADYCARDIA SYNDROME

All of the 20 patients with the tachycardia/bradycardia syndrome improved considerably on the combination of pacing and anti-arrhythmic drugs, usually both digoxin and beta-blockers. Sixteen patients became virtually symptom-free, three had occasional short bursts of tachycardia, and one became free of tachycardia but experienced a sterile reaction around two successive pacemakers, both of which had to be removed. This patient requested a further pacemaker implantation as his symptoms were so disabling and has since been well for eight months.

Generator Lifetimes

Pacemakers produced by Devices Implants (England), Cordis, Medtronic, and American Optical (U.S.A.), Elema-Schönander (Sweden), Vitatron (Holland), Biotronik (West Germany), and Sorin (Italy) were used in these patients, with the largest numbers provided by Devices and Cordis. We found no important differences in clinical use between different manufacturers' products but the data are sufficient to calculate lifetimes only for Devices pacemakers. These results are shown in fig. 1 for the fixed rate model (2970) and in fig. 2 for the demand model (3821) including the version with a magnetically operated reed switch (3821R). In each case the solid line represents the performance of the generator alone, and systems in which a normally functioning generator was removed for causes such as infection or exit block were not included. The dotted line shows the results achieved by the entire system, and every cause of cessation of pacing has been incorporated, including death of the patient, infection, electrode movement, etc. These results show that the uninterrupted pacing with the original system has continued for two years after implantation for 75% of patients with fixed rate pacemakers and for 63% of those with demand units.

Some years ago elective changing of pacemakers was undertaken at times determined on the basis of manufacturers' recommendations and our own experience. Our policy over the last three years has been to allow generators to remain in service until late changes or other indications of end of pacemaker life occur and not to replace electively. This approach can only be applied when a follow-up clinic exists, but since many units can now function for over three years elective replacement unduly curtails the life of these generators.

FIG. 1—Lifetimes of fixed-rate pacemakers (solid line) and entire pacing systems (dotted line) expressed as percentage still pacing of those which could have continued functioning at indicated time. Data is based upon 163 generators at implant, 108 at one year, 47 at two years, and 20 at 30 months.

FIG. 2—Lifetimes of demand pacemakers (solid line) and entire pacing systems (dotted line) expressed as percentage still pacing of those which could have continued functioning at indicated time. Data is based on 227 generators at implant 98 at one year, 24 at two years, and 20 at 27 months.

Premature Battery Exhaustion

Failure of a pacemaker due to battery rundown in less than 18 months is considered premature battery exhaustion, and it occurred in 28 fixed-rate units and 38 demand units over the 10-year period. The mean time of pacing in these premature failures was 14.4 months for fixed rate and 16.0 months for demand or triggered units. Most of the failures were of early models, and only one of the last 100 units replaced had premature battery exhaustion. There was no detectable difference between pacemakers produced by different manufacturers.

Follow-up Procedures

Before a patient leaves hospital the pacemaker is checked using a Nukab analyser, which displays digitally the pacing rate, the impulse duration, and the amplitude of the pacing stimulus detected from the skin electrodes on the limbs, using conventional E.C.G. leads I, II, and III. The pacemaker is checked again after one month at a special outpatient clinic and subsequently at intervals determined by the type of pacemaker and the readings obtained at the previous visit. In most cases a check is carried out one year after implantation and then at three monthly intervals until pacemaker replacement. In the case of patients who live far from the hospital arrangements are made locally for a strip of E.C.G. to be posted to the hospital where it is compared with the original record. Details of the test procedure and an evaluation of the Nukab analyser have been published previously.⁵

Our present indications for battery replacement include changes in the basic pacing rate of 5 beats/min, failure to pace when a stimulus falls during a non-refractory period, or reduction of 30% in the stimulus amplitude from limb lead electrodes in all three standard leads.

Discussion

The main indication for pacing in this series was syncope or near-syncope, which affected almost 90% of the patients and which was universally relieved. About two thirds of our cases had an abnormal axis before pacing and only one sixth had normal QRS complexes and normal axes. Recent evidence strongly suggests that bundle-branch block and an abnormal axis are precursors of complete heart block, and in many centres, particularly in the United States, pacemakers are implanted in symptom-free patients in sinus rhythm who show E.C.G. changes of this type. We did not follow this policy because it has not yet been established what proportion of such patients live a normal life span without developing complete heart block, nor how long these premonitory signs can exist before complete heart block appears. Our evidence shows that in at least some cases

many years can pass before pathological fibrosis of the conduction system develops to the stage of complete heart block. In one patient conduction block of two of the three fascicles was present for six years before pacing became necessary, and in another 11 years passed between E.C.G. evidence of disturbed conduction in one fascicle and the development of intermittent complete block. It is of course unknown how many patients with E.C.G. evidence of progressive bundle-branch fibrosis live a normal life span without developing symptoms or coming to the notice of a doctor. We regard a history of recent dizzy spells together with these E.C.G. abnormalities or a single proved Stokes-Adams attack as indications for pacemaker implantation.

The very low risk of pacemaker implantation (nil in this series,) the greatly improved prognosis compared with medical treatment, and the relief of heart failure shown in this and other series strongly support the view that all patients with complete heart block (stable or intermittent) should be considered for pacing. We have presented haemodynamic studies elsewhere⁶ showing that over half of paced patients achieve a normal cardiac output on exercise, and this is entirely compatible with the clinical improvement noted in this series. Recently increased cerebral blood flow and mental performance during pacing have also been reported.^{7, 8}

The combination of alternating supraventricular tachycardias and bradycardia is particularly difficult to treat since all drugs intended to suppress the rapid rhythms exaggerate the bradycardia and vice versa. The combination of pacing with antiarrhythmic drugs proved very successful in this and other series, and is the method of choice for such patients.^{3, 9}

The mortality in paced patients with heart block has shown a progressive decline in recent years and reports are available showing a first year mortality of 39% in St. George's Hospital, London in 1963,¹⁰ 20% in Chardack's 1965 report from Buffalo U.S.A.,¹¹ 17% in Johansson's patients from Malmö, Sweden in 1966¹² and in the combined series of 544 patients reported by Sowton in 1967,¹³ 10% in a series from Melbourne, Australia in 1971,¹⁴ and less than 5% in the present series. This encouraging trend cannot be solely attributed to improvements in apparatus and technique since the indications for pacing have changed greatly over the past 10 years. Many patients who were managed medically a few years ago now receive pacemakers, and undoubtedly patients with a good prognosis are now being paced. Since all the patients with heart block in this series had syncopal episodes or heart failure, however, it is likely that a real improvement in management had occurred.

Our figures for reliability of Devices generators (apart from complications not due to generator failure) show a fixed-rate function of 100% after one year and of 90% after two years. After 30 months service 75% were still functioning normally. Demand pacemaker figures were 96% after one year and 84% after two years. This greater reliability of fixed-rate over demand generators is common to all manufacturers and would be expected from the differences in circuit complexity and current drain from the batteries.

The results are similar to those from other centres. Davies *et al.*¹⁵ found 99% of Devices fixed-rate generators functioning at one year and 77% at two years. Corresponding figures for demand units were 89% at one year and 70% at two years. McDonald and Layton¹⁶ reporting only on the fixed rate unit model 2970 found 84% functioning at two years and 65% at three years after implantation.

Our results compare well with published data for alternative equipment. The Cordis Corporation report normal function at two years as 48% for model 111B, 65% for model 111C, and 83% for model 111G J. The figures for R-wave inhibited Cordis demand pacers (Stanicor) are 73% at two years and for R-wave triggered units (Ectacor) 35%.¹⁷

Corresponding figures for the present types of Medtronic units are not available because insufficient time has elapsed since their introduction, but a limited comparison between entire pacing systems, including generator and electrode as well as problems such as infection or wire breakage, is possible. Green¹⁸

reported 71% of model 5870C (fixed-rate) still functioning at 24 months and after 30 months 34% were still functioning, compared with 58% for Devices model 2970. The performances of Devices 3821 and Medtronic 5841 demand systems were virtually the same after 24 months service.

Most of the complications now occurring are related to medical, mechanical, or biological factors (infection, electrode movement, high thresholds, etc.) but the high incidence of pacing failure before battery depletion (43%) in Britain reported only a few years ago¹³ has been greatly reduced. Our experience with treatment of infected pacemakers supports reports from other centres that it is sometimes possible to cure this complication without removing the pacemaker.^{19, 21} We regard some follow-up system as mandatory, and it has been widely reported that pacemaker emergencies have become rare when follow-up checking at special clinics is available.^{5, 22-25} Throughout 1974 only 7% of our patients having replacement pacemakers were admitted urgently through the casualty department. The remaining 93% of impending pacemaker failures were detected in advance and the patient admitted via the pacemaker clinic. Though the incidence of heart block in Britain is similar to that in Europe²⁶ the frequency with which patients are paced is many times less than in other European countries. In a world-wide survey covering 1972 pacemakers were implanted into new patients at the rate of over 120/per million population in Sweden and 100-120 per million in West Germany.²⁸ A figure of over 80/per million for France can be calculated from data given by Besse and Lardeau.²⁹ The figure for the British Isles was 22 per million.³³ Hence probably the number of paced patients in the U.K. will increase considerably over the next few years.

Conclusions

In our series of 372 patients treated with pacemakers during a 10-year period there was no mortality associated with implantation, and the subsequent mortality is now less than 5% a year. About 85% of the patients were paced because of syncope, and we regard a single Stokes-Adams attack as a firm indication for pacing. We do not implant pacemakers in symptom-free patients on the basis of E.C.G. evidence of delayed conduction only.

The reliability of Devices generators (excluding electrode movement or infection) now in use results in continuing function at two years of 90% for the fixed-rate model 2970 and 84% for the demand model 3821. About 75% (fixed rate) or 60% (demand) of patients continued uninterrupted pacing with the original system two years after implantation.

We thank the many physicians who referred cases for pacing and in particular we thank Dr. Deuchar at Guy's Hospital for his help. We also thank Miss Alison Shennon, pacing technician, Guy's Hospital, and the many registrars and Fellows involved for their contributions.

P. Roy was supported by a Fellowship from the Postgraduate Committee, University of Sydney.

References

- Rosenbaum, M. B., *et al.*, *American Heart Journal*, 1969, 78, 450.
- Lev, M., *American Journal of Medicine*, 1964, 37, 742.
- Sowton, E., Spurrell, R., and Roy, P., *Proceedings of International Symposium on Conduction Disturbances*, Porto, 1973. Basel, Karger.
- Roy, P., and Sowton, E., *British Medical Journal*. In press.
- Sowton, E., and Gray, K., *Thorax*, 1971, 26, 145.
- Sowton, E., and Flores, J., *Bulletin of the New York Academy of Medicine* 1971, 47, 999.
- Shapiro, W., and Chawla, N., *Circulation*, 1969, 40, 863.
- Lagergren, K., *British Heart Journal*. In press.
- Kaplan, B. M., *et al.*, *American Journal of Cardiology*, 1973, 31, 497.
- Sowton, E., M.D. Thesis, University of Cambridge, 1964.
- Chardack, W. M., *et al.*, *Surgery*, 1965, 58, 915.
- Johansson, B. W., *Acta medica Scandinavica*, 1966, 180, suppl. No. 451.
- Sowton, E., *British Medical Journal*, 1968, 1, 11.
- Lippis, H., Anderson, S. T., and Pitt, A., *Medical Journal of Australia*, 1971, 1, 573.
- Davies, E. T. L., Hanson, P. T. G., and Bassett, H. F. M., *British Heart Journal*, 1973, 35, 865.
- McDonald, A., and Layton, C., *British Heart Journal*, 1973, 35, 1941.

- ¹⁷ Cordis Corporation, *Technical Memorandum*, PVI, 25th July 1973.
¹⁸ Green, G. D., *Chemistry and Industry*, 1974, In press.
¹⁹ Furman, S., *Annals of Thoracic Surgery*, 1972, 14, 328.
²⁰ Bonchek, L. I., *Annals of Surgery*, 1972, 176, 686.
²¹ Dieter, R. A., et al., *Geriatrics*, 1973, 28, 78.
²² Green, G. D., et al., *British Heart Journal*, 1969, 31, 707.
²³ Thalen, H. J. T., et al., *Annals of the New York Academy of Sciences*, 1969, 167, 515.
²⁴ Parsonett, V., et al., *American Journal of Cardiology*, 1970, 25, 311.
²⁵ Edhag, O., et al., *British Heart Journal*, 1971, 33, 185.

- ²⁶ Eraut, C. D., Evans, R. C., and Shaw, D. B., *British Heart Journal*, 1973, 35, 557.
²⁷ Karlof, I., and Lagergren, H., in *Cardiac Pacing. Proceedings of the 4th International Symposium*, 1974, ed. J. Thalen, p. 84, Van Gorcum.
²⁸ Sykosch, H. J., *Cardiac Pacing. Proceedings of the 4th International Symposium*, Groningen, 1974, ed. J. Thalen, p. 95, Van Gorcum.
²⁹ Besse, P., and Lardeau, P., in *Cardiac Pacing. Proceedings of the 4th International Symposium*, 1974, ed. J. Thalen, p. 90, Van Gorcum.
³⁰ Sowton, E., in *Cardiac Pacing. Proceedings of the 4th International Symposium*, 1974, ed. J. Thalen, p. 109, Van Gorcum.

Hospital Topics

Fever in the Neutropenic Patient

K. ATKINSON, H. E. M. KAY, T. J. McELWAIN

British Medical Journal, 1974, 3, 160-161

Summary

A total of 100 consecutive episodes of fever of 101° F (38.3°C) or above in 56 neutropenic patients have been investigated. All the patients had either acute leukaemia or aplastic anaemia. A cause for the fever was found in 68 of these episodes, in 87% of which it was due to infection. The commonest single finding was septicaemia (30 episodes). Only two episodes of fever could be ascribed solely to the underlying malignant disease.

Infection should be assumed to be present and the cause of fever in neutropenic patients until proved otherwise.

Introduction

As a result of the increasing use of cytotoxic chemotherapy and radiotherapy for malignant disease neutropenia is common. Fever in the neutropenic patient is a difficult problem. In a group of 56 patients with a neutropenia of 1,000/mm³ or less we have investigated 100 consecutive episodes of fever of 101° F (38.3° C) or more to determine the cause.

Patients and Methods

The patients had either acute leukaemia or aplastic anaemia (table I) and were nursed in the reverse barrier unit at this hospital during their illness. All had a neutropenia of 1,000/mm³ or less, and in most cases the count was less than 100/mm³. Any patient was investigated whose temperature reached 101° F (38.3° C) at two consecutive four-hourly intervals or 101° F twice in 48 hours or 102° F (38.3° C) or above on one occasion. The routine procedure was: careful physical examination, the performance of two or three sets of blood cultures (5 ml blood in 50 ml glucose broth, 3 ml in 20 ml broth in a Castaneda's medium bottle, and 1 ml in 10 ml Robertson's meat broth),

examination of a midstream specimen of urine, and chest x-ray examination. If the fever did not settle after four days (with or without the use of antibiotics) the blood was examined for the presence of atypical "viral" lymphocytes and the urine for cytomegalovirus cells. In addition viral serological tests with paired serum were done.

TABLE I—Underlying Disease in 100 Consecutive Febrile Episodes

	No. of Episodes
Acute myeloblastic leukaemia	46
Acute lymphoblastic leukaemia	18
Acute undifferentiated leukaemia	14
Blast transformation of chronic myeloid leukaemia	8
Lymphosarcoma cell leukaemia	5
Aplastic anaemia	9

Results

A cause of the fever was determined in 68 episodes (table II). There was a definite cause in 66 and a probable cause in two. Though the largest single group was one in which no cause was found (32 episodes) the commonest single cause (30 episodes) was septicaemia with a positive culture. (Gram-negative bacteria in 17, Gram-positive bacteria in 12, and a fungus in 1). The second commonest cause was pneumonia (11 episodes), followed by blood transfusion (6) and urinary tract infection (5). One of the two perioral infections started as a pustule growing *Staphylococcus aureus*, while the other started as a typical herpes simplex vesicle. In spite of appropriate treatment both went on to cause extensive perioral and perinasal crusting with severe tissue necrosis. There was one episode of fever in which no abnormality other than severe aphthous-like mouth ulcers was present; these grew no abnormal organisms.

Only two episodes of fever could be attributed with certainty to the underlying malignant disease rather than to any asso-

TABLE II—Cause in 100 Consecutive Febrile Episodes

	No. of Episodes		No. of Episodes
No cause found	32	Active malignant disease	2
Septicaemia	30	Pelvic abscess	1
Pneumonia	11	Bartholin's abscess	1
Blood transfusion	6	Cellulitis	1
Urinary tract infection	5	Boils	1
Cytomegalovirus infection	3	Candida oesophagitis	1
Intravenous infusion site infection	3	Mouth ulcers	1
Perioral infection	2		

Leukaemia Unit, Institute of Cancer Research, Royal Marsden Hospital, Sutton, Surrey

K. ATKINSON, M.B., M.R.C.P., Lecturer in Medicine
H. E. M. KAY, M.D., F.R.C.PATH., Consultant Clinical Pathologist
T. J. McELWAIN, M.B., M.R.C.P., Consultant Physician