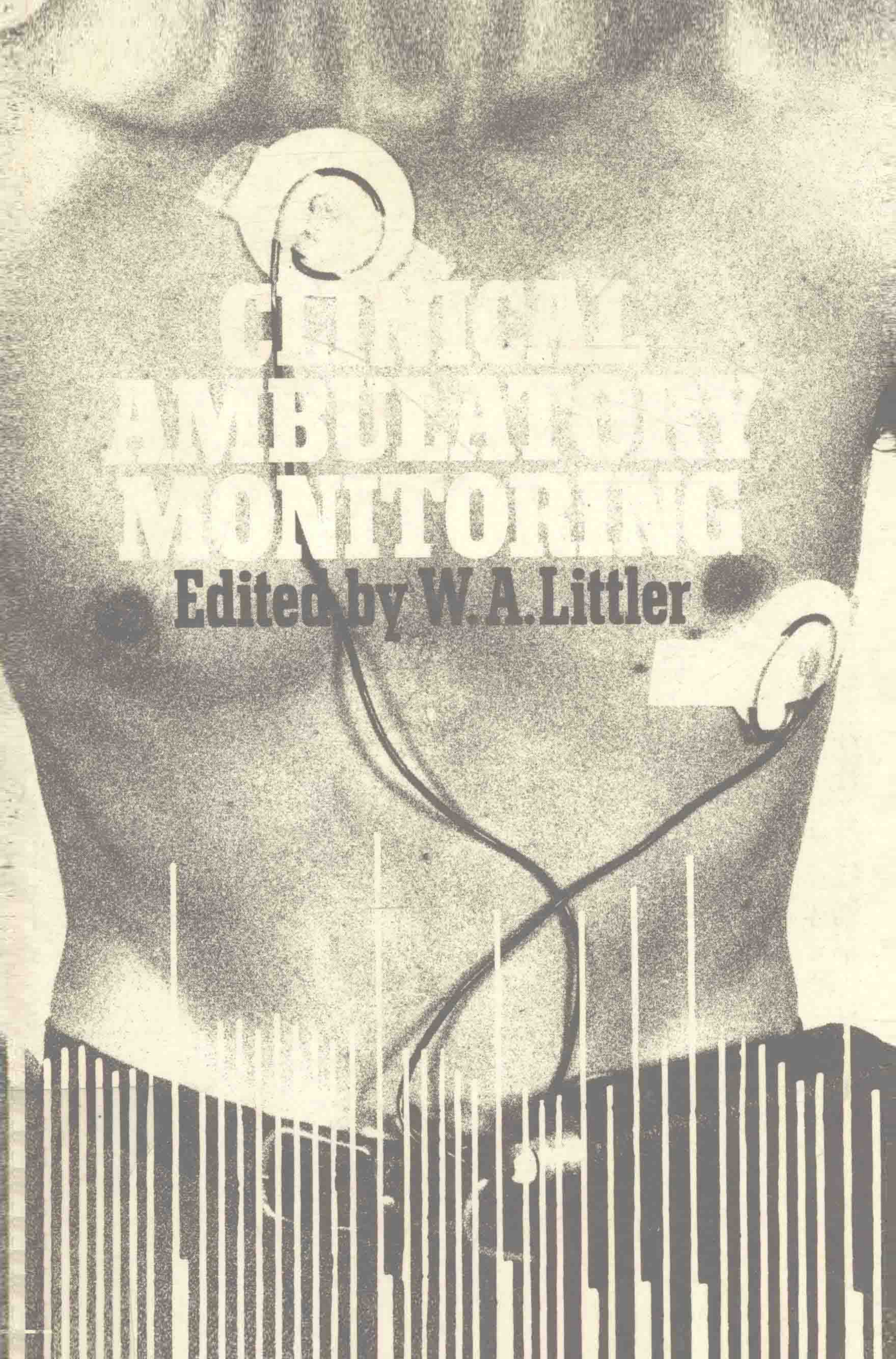
CLINICAL
AMBULATORY
MONITORING
Edited by W. A. Littler

CLINICAL AMBULATORY MONITORING

edited by

W. A. LITTLER
M.D., F.R.C.P.

*British Heart Foundation
Professor of Cardiovascular Medicine,
Birmingham University
and Honorary Consultant Cardiologist,
Birmingham Area Health Authority*

1980
LONDON
CHAPMAN AND HALL
150TH ANNIVERSARY

First published 1980
by Chapman and Hall Ltd.,
11 New Fetter Lane,
London EC4P 4EE

Printed in Great Britain at the
University Press, Cambridge

ISBN 0 412 15830 2

British Library Cataloguing in Publication Data

Clinical ambulatory monitoring.
1. Ambulatory medical care
2. Patient monitoring
I. Littler, W. A.
616.07'54 EA974

ISBN 0-412-15830-2

Goodman, L. S., and Gilman, A. (Eds.): The Pharmacological Basis of Therapeutics. 4th Ed., New York, Macmillan, 1970, p. 1149.
Grant, W. M.: Toxicology of the Eye. 2nd Ed., Springfield, Charles C Thomas, 1974, pp. 1069–1070.
LeJeune, J. R.: Les oligo-elements et chelateurs. Bull. Soc. Belge Ophtalmol. *160*:241, 1972.
Walsh, F. B., and Hoyt, W. F.: Clinical Neuro-Ophthalmology. 3rd Ed., Baltimore, Williams & Wilkins, Vol. III, 1969, pp. 2594–2596.

* * * * * * * * * * * * *

Class: Anthelmintics

Generic Name: 1. Antimony Lithium Thiomalate; 2. Antimony Potassium Tartrate; 3. Antimony Sodium Tartrate; 4. Antimony Sodium Thioglycollate; 5. Sodium Antimonylgluconate; 6. Stibocaptate; 7. Stibophen

Proprietary Name: 1. Anthiomaline (G.B.); 2. Antimonial Wine (G.B.); 3. Antimony Sodium Tartrate; 4. Antimonio E Sodio Tioglicolato (Ital.); 5. Triostam (G.B.); 6. Astiban; 7. Fuadin

Primary Use: These trivalent antimony compounds are used in the treatment of schistosomiasis and filariasis.

Ocular Side Effects

A. Systemic Administration
   1. Eyelids or conjunctiva
      a. Edema
      b. Urticaria
   2. Yellow discoloration of skin or sclera
   3. Decreased vision
   4. Pupils
      a. Mydriasis
      b. Absence of reaction to light
   5. Papilledema
   6. Optic atrophy
   7. Blindness
   8. Subconjunctival or retinal hemorrhages secondary to drug-induced anemia

Clinical Significance: Since antimonials are rarely used in developed countries, only limited data on their complete toxicologic effects are available. While the preceding adverse reactions have been reported, few are well documented. Serious adverse ocular reactions have been seen, although infrequently.

PREFACE

In the last few years, ambulatory monitoring has passed from a research phase to an established, evaluated and costed clinical investigation. This is particularly so in its application to the field of cardiovascular medicine. The real breakthrough came with the development and sophistication of miniature tape-recording systems, starting in the 1960's with Dr Norman Holter and Dr Frank Stott. Such a system allows greater freedom for both the patient and the doctor concerned. It allows an individual to be studied in his home environment and a great deal more data can be generated. In each 24-hour period at least 100 000 heart beats are recorded which allows a great deal of versatility in terms of data processing.

Electrocardiography has been exploited more than any other variable but more recently arterial blood pressure, electro-encephalography and measurement of physical activity have been added to ambulatory monitoring programmes, thus, widening the scope of their clinical application. *Pari passu* with the development of the recording apparatus has been the development of automated analysis systems which are essential for the full realisation of the advantages of ambulatory monitoring.

This book provides a review of the present situation in ambulatory monitoring as applied to clinical practice. It deals with the development of tape-recording and analysis systems and indicates what is presently available and which particular apparatus is most suitable in any given clinical situation. Techniques of electrocardiographic recording are dealt with in some detail in relation to the diagnosis and management of arrhythmias, conduction disturbances and ischaemic heart disease. There is a section on arterial pressure recording and its relation to our understanding of the physiological mechanisms and also its use in the management of difficult problems of high blood pressure. Continuous recording of the electroencephalogram is proving increasingly useful to neurologists and its wider application is dealt with in a separate section.

Finally, the recording of physical activity is dealt with.

This book hopes to provide the reader with a standard account of each individual technique providing him with the various choices of apparatus that are currently available and indicating which particular system might have an advantage for a special clinical situation.

W. A. L.
Birmingham

CONTENTS

Contributors vii

Preface ix

1 Ambulatory tape recording 1
J. R. W. Morris and A. F. Simpson

2 ECG Data Analysis Systems 27
L. Goulding

3 Electrocardiography 69
A. J. F. Page

4 Continuous ambulatory monitoring of direct arterial pressure 96
W. A. Littler

5 The contribution of ambulatory EEG to the management of epileptic patients 122
J. R. Ives and J. F. Woods

6 Monitoring physical activity 148
E. J. Bassey and
P. H. Fentem

Index 173

1 AMBULATORY TAPE RECORDING

J. R. W. Morris and A. F. Simpson

Medical diagnostic techniques are devised to make apparent symptoms which are not revealed by inspection or palpation. To this end, the art of medical history taking has been developed to the point that, in some circumstances, it remains the primary diagnostic contributor.

Many disease processes show symptoms only intermittently and there is frequently a possibility of these symptoms being modified by the patient's presence in a hospital or clinic. The natural solution to these problems is to devise means for observing symptoms outside the clinic, preferably continuously – ambulatory monitoring.

1.1 FIRST AMBULATORY RECORDING

The first recorded instance of ambulatory monitoring of which this author is aware is 1873 and although the Marey brothers, designers of the system, are well known for their contribution to cardiovascular medicine, this experiment concerned the recording of pressure under the foot. A fluid-filled sac was built into the sole of a shoe and connected by a rubber hose to a transducer (whose design is not recorded). This transducer drove the pen of a smoked-drum cymagraph which was driven by clockwork and carried by the subject of the experiment. All the essential features of a modern ambulatory recorder are present in the design; a transducer, a portable power source, and a permanent record. The design also presumably suffered many of the same problems as today's recorders; the measurement process disturbed the measured process, the apparatus was too large to be worn with comfort, the power supply did not last long, and the subject's movements undoubtedly introduced artefacts onto the recording.

1.1.1 Radiotelemetry

The ECG, because of the ease with which it can be detected and its considerable diagnostic value, as an obvious candidate for both static and ambulatory recording. The first recordings of ECG away from the constraints of a fixed ECG machine used radio-telemetry.

Portable radio transmitters were developed during the Second World War for field telegraphy and voice communication. Any channel capable of transmitting voice can easily be modified for transmitting ECG, but the redundancy of information in human speech means that intelligible transmission is possible in circumstances where the quality of ECG would be severely degraded. The uncertainty of transmission quality proved to be the main reason why radio-telemetry of ECG and other physiological signals never came into widespread use. Even within a hospital it is particularly difficult to organize high quality ECG transmission because of the metal structure within the building and the numerous other sources of radio frequency interference – diathermy, X-ray machines, paging systems and electromechanical devices being switched on and off. There are special circumstances where radio transmission is appropriate, such as coronary care and obstetric wards, but in these instances the patient is generally constrained to stay within the ward or else elaborate receiver aerials need to be installed throughout the hospital.

1.1.2. Early recorders

Tape recording of physiological signals is now the means by which long-term ambulatory monitoring is achieved, but tape recording technology has only recently reached a point where this becomes a practical proposition.

The development of tape recorders is in many ways contemporary with and analogous to the development of television. Both techniques began during the nineteen thirties in forms which are scarcely recognisable as the precursors of today's instruments. Baird's mechanically-scanned televisions appeared in the homes of the most enthusiastic of technical hobbyists and many of these homes also contained large, elaborate wire recorders. Later in this chapter the basic principles of recording are explained and the properties of suitable recording media are shown to be ferromagnetism and dimensional stability. The first suitable material to be found was ferromagnetic wire. The resolution of magnetic regions on the wire was extremely coarse and it was therefore moved quite rapidly across the recording and replay heads.

In spite of the technological problems which existed, portable wire recorders were built and used with great skill most notably by ornithologists and other naturalists to record the sounds of nature. The recordings were of excellent quality but the total recording time was necessarily short.

The move from wire to tape as a suitable recording medium was an important conceptual step forward. Tape recording now provides a greater volumetric density of information storage than any other technique, solid-state technology not excepted. The reason is simply explained. With tape, a recording is made in two dimensions (as in solid-state memory) but the tape is then rolled up to become, in effect, a three dimensional medium. The implications of this are explored later in the chapter.

The first tape recorders became widely available early in the nineteen fifties and some standards were agreed for tape size and recording speeds. Fifteen inches per second and quarter inch width tape allowed high fidelity recording of music. In parallel, tape recorders were developed for scientific purposes and standards in this area were laid down by the Inter Range Instrumentation Group (IRIG) in the USA which was concerned with the recording of radio telemetric signals from experimental missiles. The IRIG standards specify tape speeds which are multiples of 15 i.p.s. and modulation characteristics for frequency modulation.

1.1.3. Early ambulatory ECG

The pioneer of ambulatory tape recording of ECG was Holter in USA who devised a portable recorder based on quarter inch tape running at $\frac{1}{16}$ inch per second. The 500 feet of tape was wounded on 2.65 inch spools and the apparatus ran for 24 hours. Largely because it used pre-transistor electronics, the recorder weighed several pounds and had to be carried on a shoulder strap – not an instrument for the old or infirm. This instrument was taken up by Del Mar Avionics Inc. and its descendants became the most widely used type of recorder in the 1970s.

At around the same time, the MRC in Great Britain developed a means for recording heart rate averaged over long time periods. The Socially Acceptable Monitoring Instrument (SAMI) used an electrochemical cell in which known, fixed amounts of a metal ion were deposited on a cathode for each detected heart beat. The cell could be read back by noting the total amount of electric current necessary to remove the metal ion. Although this instrument provided some useful epidemiological information, it proved no match for tape recording, in spite of its very small size.

1.1.4. Early ambulatory blood pressure

Quite separately from Holter's developments in USA, Stott in Oxford developed during the 1960s recorders for long-term monitoring of blood pressure. After initial experiments with light intensity modulation of slowly-moving photographic emulsion tape, the appearance of the Philips Compact Cassette in the early 1960s provided a new format for tape recording which appeared ideally suited to ambulatory monitoring. Since the cassette is now by far the most widely used tape format for ambulatory monitoring, it is worthwhile examining it in some detail.

1.1.5. Cassettes

Early recording tape used an acetate base, taking the plastics technology from the film industry. Acetate tape has one considerable flaw. While quite tough, it is subject to both elastic and plastic deformations which cause distortions for reasons which are explained later in the chapter. This problem is made proportionately worse as the acetate base is made thinner. The introduction of a polyester tape base allowed thinner tape to be made and more of it to be wound onto spools of the same size. Philips noted that the public seemed prepared to spend large sums of money on cheap transistor radios which produced very low fidelity music. The Compact Cassette was developed as the recording component to this area of the electronics market. Narrower tape (3.75 cm) and a tape speed ($1\frac{7}{8}$ i.p.s.) far lower than was normally used for music were specified. The recording surface was moved to the convex side of the tape so that the head could press against a cheap pressure pad built into the cassette. The development of this simply conceived medium is well known. It has now effectively displaced reel-to-reel recording of music, is used as a digital storage medium on computers, and has been adopted by every ambulatory monitoring recorder manufacturer except Avionics and its imitators. It seems likely to remain the most convenient tape format for many years to come.

1.2 PRINCIPLES OF TAPE RECORDING

1.2.1. Fundamentals

Tape recording relies on the ability of certain magnetic materials, when exposed to a magnetic field, to retain some magnetism even after the original magnetising field is removed. This property is known as magnetic hysteresis. The most common application of such materials is for so called 'permanent magnets'. A magnetic material exhibiting this property is said to be 'magnetically hard', whereas a material which looses its magnetism as soon as the applied field is removed is said to be 'magnetically soft'.

In the recording process a tape coated with a magnetically hard material is passed over a 'recording head'. The recording head consists of a magnetically soft core with a coil wound on it. There is a small 'gap' in the core at the surface in contact with the tape. When current is passed through the coil the magnetic flux induced in the core produces a high field strength across this gap, which in turn causes flux to penetrate the magnetic coating of the tape. Because this coating is magnetically hard it retains some magnetism after it has moved away from the high field region of the gap. Hence if an alternating current is passed through the coil while the tape is moved over the surface of the head, an alternating sequence of north and south poles will be left on the tape.

If the tape is now passed over a similar head (with an un-energized coil), the changing flux on the tape will induce a voltage into the coil. In this way the original information can be relayed.

It is important to note the distinction between the recording and replay processes. In the former the flux produced on the tape is proportional to the current in the coil, whereas in the latter the recovered voltage is proportional to the rate of change of flux.

This has several important effects. Firstly it means that the output voltage will be directly proportional to the recovered frequency (assuming a constant flux on the tape). In order to obtain a constant overall frequency response it is necessary to compensate for this by means of an 'equalization' circuit having a gain inversely proportional to frequency.

An extension of this argument leads to the conclusion that it is impossible to recover a DC signal from tape with a conventional replay head since such a signal would produce a zero rate of change of flux as it passed over the head.

In practice the lowest recoverable frequency with a conventional replay head is limited to approximately 4 Hz by amplifier considerations. Below this frequency the signal from the replay head becomes small by comparison with the noise of the first amplifying stage in the replay equipment. To go below this limit requires the use of a special large replay head.

It is important to note that this frequency limit refers to the actual frequency recovered at the replay head, not to the frequency recorded at the record head. These two frequencies need not be the same if the tape is run at a different speed for record and replay. Thus it is possible for a physiological recorder to record signals down to a fraction of a Hz and for these to be replayed by running the tape over the replay head at a much higher speed than that used in the recorder. The ratio of replay speed to record speed is termed the speed-up ratio.

For physiological purposes a high speed-up ratio confers two advantages. Firstly it allows the recovery of low frequency signals for the reasons given above; but secondly, and more importantly it allows recordings made over a long time to be assessed in a short time.

Current ambulatory monitoring practice is to use a speed-up ratio of 60 or 120.

1.2.2. *Recorded wavelength*

Because a wide variety of different record and replay speeds are in use for various applications, it is useful to be able to compare systems in terms of what is actually recorded on the tape. This can best be done by means of the wavelength of the signal as it appears on the tape. The recorded wavelength is the length of tape passing past the recording head during one complete cycle of the input waveform. Hence, it represents the distance between successive north poles on the tape.

Using this concept it is easy to see that a 100 Hz signal recorded on tape at a speed of 2 mm/s, produces the same flux pattern on the tape as a 2380 Hz signal recorded at 47.6 mm/s. In both cases the recorded wavelength is 0.02 mm.

1.2.3. *High frequency limitations*

The highest frequency which can be successfully recorded and replayed is normally limited by the dimensions of the replay head and the particle size of the magnetic coating on the tape. As the gap width of the replay head approaches the recorded wavelength on the tape the output signal rapidly falls to zero. A similar loss of output occurs when the mean particle size becomes comparable with the recorded wavelength. A third mechanism limiting the high frequency response is the self-demagnetization which occurs when the recorded wavelength becomes very short. This is directly related to the coercivity of the tape (see below).

Since all these high frequency limitations are directly related to the recorded wavelength, the high frequency performance can be raised to any required limit by suitably raising the tape speed. The only penalty is that more tape is needed for a given recording time. For a given tape head there will be an absolute high frequency limit when the capacitance of the windings becomes dominant. However by a suitable design of the head it is possible to record frequencies up to 10 MHz if a sufficiently high tape speed is used.

1.2.4. *Low frequency limitations*

Two factors limit the useful low frequency performance of a record/replay system. One is the proportional relationship between recovered signal amplitude and frequency referred to above. This combined with the inevitable noise introduced by the first amplifying stage following the replay head, limits the frequency at some point where the recovered signal to noise ratio becomes unacceptably low.

The second limiting factor arises when the recorded wavelength on tape becomes comparable with the total length of the replay head pole-face in contact with the tape.

This results in a series of ripples in the low frequency response, with the head output rising to a maximum when the pole-face length is equal to twice the recorded wavelength and falling to zero when the two are equal.

Both of these limitations can be overcome to some extent by the use of a suitably large replay head. This can accommodate long pole faces and a large coil, thus lowering the frequency at which wavelength effects become significant and increasing the overall output voltage.

1.3 PROPERTIES OF TAPE

Magnetic recording tape consists of a flexible backing coated with a thin layer of magnetic material. Recorded information is stored on the tape as a pattern of varying magnetisation in the coating. In a typical C120 cassette tape the backing is a 6 micron thick polyester film which is coated with a 3 μm-thick layer of iron oxide, giving an overall thickness for the tape of 9 μm.

The oxide chosen for the tape coating (usually gamma iron oxide) is magnetically hard, i.e. it exhibits magnetic hysteresis. It is only by virtue of its hysteresis that magnetic tape can be used as a storage medium for information. The magnetic properties of a material can best be represented by means of a plot of magnetisation against applied field strength. Figure 1.1. shows such a hysteresis curve for a typical tape coating. Two parameters of interest may be measured from this curve: the Remanence (R) and the Coercivity (C). The former provides a measure of the maximum magnetisation which can be retained by the tape whilst the latter indicates the strength of the reverse field necessary to reduce the remanent magnetisation to zero. When high frequencies are recorded on a tape an alternating pattern of closely spaced reversals of magnetic flux is left on the tape. Each of these therefore acts as a demagnetising field for its neighbour. This effect is known as self-demagnetisation and can be a limiting factor in the high frequency performance of a tape. High coercivity is desirable in a tape if self-magnetisation is to be minimised. A final feature of interest in the hysteresis curve is the overall shape of the curve. A curve such as that shown in Fig. 1.1 has a relative large

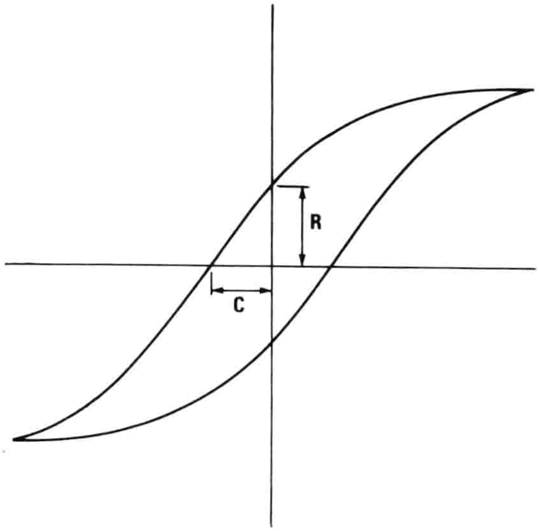

Fig. 1.1 Hysteresis curve for a typical tape.

range of applied field over which there is an approximately linear relationship between applied field and resulting magnetisation. The rather 'squarer' curve shown in Fig. 1.2 on the other hand has a much smaller range of applied field over which this linear relationship holds. A tape with this latter characteristic would be less suitable for a direct recording system where the tape is required to have a linear relation between applied signal and resulting magnetisation. It would however be perfectly suitable for a carrier of a digital system. It should be noted however that a squarer hysteresis curve does not of itself imply that a tape will perform better on a carrier or digital system. Any improvement in performance will only be obtained if the change to a squarer characteristic produces an increase in either the remanence or the coercivity of the tape. This was the case in the early days of magnetic recordings. However recent improvements in tape technology, resulting largely from the demands of the audio market, have produced a tape which combines a high coercivity and remanence with an acceptably linear transfer characteristic. Such a tape can provide optimum performance in both direct and carrier recording systems.

An important parameter affecting the performance of the tape is the thickness of the magnetic coating. It seems logical that a tape with a thick oxide coating should be capable of providing more output than one with a thin coating. However, this is only true at low frequencies. At higher frequencies only those regions of oxide

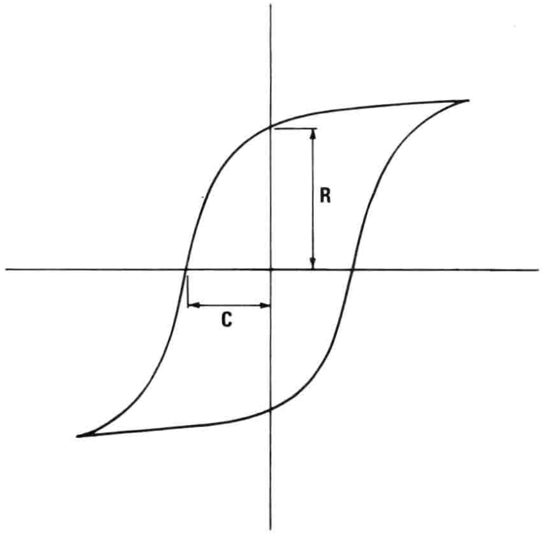

Fig. 1.2 Squarer Hysteresis curve.

close to the surface contribute to the replayed signal and hence a thick coating will provide no more output than a thin one. Hence a tape with a thick coating will tend to provide more output at low frequencies than one with a thin coating but its output will fall off more rapidly at higher frequencies. This thickness effect starts to become significant when the thickness of the coating approaches the recorded wavelength on tape. (At $1\frac{7}{8}$ i.p.s. a signal of 15 KHz has a recorded wavelength of approximately 3 μm.)

1.3.1 Bias

The very hysteresis which makes magnetic tape recording possible, also results in it being non-linear process. Thus small applied magnetic fields produce no change in the magnetisation of the tape. To obtain a linear recording it is necessary to 'bias' the tape into the region on the hysteresis curve where there is an approximately linear relationship between applied field and resulting magnetisation. This can most simply be achieved by passing a direct current through the recording head, with the signal to be recorded superimposed as small fluctuations in this current. This technique is known as DC bias. Although simple in concept it has some serious disadvantages. Effectively only half the total magnetisation range of the tape is used, since the tape will always be biased to one side of the hysteresis curve. More seriously the tape will be left magnetised even with zero input signal. Since the tape coating consists of discrete particles it can never be perfectly uniform. Hence as the magnetized tape is replayed there will be random signals induced in the replay head. This gives rise to the effect known as tape-hiss on audio recorders. The level of hiss from magnetised tape is several times greater than that obtained from the same tape in an unmagnetized state.

To overcome these disadvantages of DC bias it is customary to use AC bias. In this technique a high frequency alternating current is passed through the recording head such that the field applied to the tape alternates between the two linear regions of the hysteresis curve. The signal to be recorded is again superimposed on this bias signal. The bias frequency chosen is much higher than can be recorded on the tape at the speed in use so that no residual magnetisation is left on the tape (i.e. the tape self magnetizes at the bias frequency). This results in no net magnetisation of the tape and therefore much lower levels of tape hiss. Moreover the use of AC bias employs both halves of the tape hysteresis curve thereby enabling a larger output signal to be obtained from a given tape, than is possible with DC bias.

1.4 TYPES OF SIGNAL

A recorder for ambulatory use may be required to record a variety of different physiological signals. They may be loosely divided into two classes: 'AC' signals and 'DC' signals. Different recording methods must be used to handle these two classes of signal. The available recording methods are described in more detail below.

'AC' signals are those where the mean (DC) value of the parameter being measured is not important and where that parameter changes only slowly. Body temperature is an obvious example of this type of parameter.

1.4.1 Direct recording

In direct recording, as the name implies, the signal being recorded is applied directly to the recording head (after suitable amplification). The advantage of this method is that it allows the full high frequency range of the tape recording process to be used for the signal and thus gives the best possible HF response of all the methods described. Its limitations are that it cannot be used to record DC and that the amplitude of the signal recovered from tape depends directly on the magnetic properties of the tape and hence may vary between tapes of different types. Bias (normally AC bias) must always be used with direct recording to obtain linear recording. An ambulatory cassette recorder capable of recording for 24 hours continuously might be capable of a frequency response of

0.15–100 Hz when used for direct recording at 2 mm/s tape speed. A typical bias frequency for such a recorder would be 10 KHz.

1.4.2 Carrier recording

In carrier recording, the signal to be recorded is modulated onto a carrier frequency which is in turn recorded on the tape. When the tape is replayed the recovered carrier must be demodulated in order to obtain the original signal.

The advantages of using a carrier are that signals down to DC may be recorded and recovered and that the amplitude of the recovered signal is independent of the properties of the tape. The disadvantages are that there is a limit to the highest frequency which may be recorded and that fluctuations in tape speed (flutter) may appear as noise on the recovered signal. The severity of the high frequency limit and the effect of speed fluctuations both depend on the modulation method employed. The signal frequency must always be less than the carrier frequency and the latter must be less than the frequency limit of the tape, since the modulation process creates side-bands at frequencies above and below the carrier, which must also be recorded. The two most common modulating methods used are Mark/Space (M/S) ratio modulation and Frequency Modulation (FM). In the former the signal is used to vary the mark/space ratio of a constant frequency carrier, whilst in the latter the signal varies the frequency of the carrier. For a given carrier frequency M/S modulation can only handle half the signal frequency of FM. (This is best understood by considering that for FM both positive and negative edges of the carrier provide information about the signal whereas for M/S modulation alternate edges are fixed in time by the constant carrier frequency and therefore convey no information.) However M/S modulation has the advantage of being relatively immune to tape speed fluctuations at frequencies below the carrier frequency. To obtain a similar immunity on an FM system requires that a constant frequency signal is recorded on a separate tape track. This 'flutter-compensation' track can then be used to correct for speed fluctuations on one or more signal tracks.

When using a carrier recording system the tape is only required to record transitions of the carrier and therefore need not operate on a linear region of its transfer characteristic. For this reason it is not necessary to use bias. However there may be cases where the use of AC bias can be an advantage and both types of system will be found in practice.

In principle all physiological signals could be recorded on a carrier system, whether they fall into the 'AC' or 'DC' categories referred to above. Indeed this is the method normally employed on