

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

WORLD HEALTH ORGANIZATION

TECHNICAL REPORT SERIES

No. 231

ARTERIAL HYPERTENSION AND ISCHAEMIC HEART DISEASE

PREVENTIVE ASPECTS

Report of an Expert Committee

	Page
1. Introduction	3
2. Prevention and control of arterial hypertension	4
2.1 Terminology and classification	4
2.2 Methodology of blood pressure determination	4
2.3 Diagnosis	6
2.4 Stages of essential hypertension	6
2.5 Renal hypertension	10
2.6 Preventive and therapeutic measures	11
2.7 Research aspects	14
3. Prevention and control of ischaemic heart disease	16
3.1 Terminology and classification	16
3.2 Diagnostic criteria	17
3.3 Preventive and therapeutic measures	19
3.4 Research aspects	23
4. Summary and conclusions	24
Annex 1. Methodology of renal investigation in arterial hypertension	26
Annex 2. Differential diagnosis of essential and renal hypertension	27

WORLD HEALTH ORGANIZATION

GENEVA

1962

**EXPERT COMMITTEE ON
ARTERIAL HYPERTENSION AND ISCHAEMIC HEART DISEASE**

Geneva, 16-23 October 1961

Members :

Dr J. Brod, Associate Professor of Medicine ; Vice-Director, Institute for Cardiovascular Research, Prague, Czechoslovakia

Dr H. E. Hilleboe, Commissioner of Health, Department of Health of the State of New York, Albany, N.Y., USA

Professor N. Kimura, Director, Third Department of Internal Medicine, and Director, Research Institute for Cardiovascular Diseases, Kurume University Medical School, Kurume-shi, Kyushu, Japan

Dr J. Lenègre, Professeur de Médecine, Clinique médicale à la Faculté de Paris, Hôpital Boucicaut, Paris, France

Professor A. L. Myasnikov, Director, Institute of Therapy, Academy of Medical Sciences, Moscow, USSR

Dr V. Puddu, Director, Centre for Cardiovascular Diseases, Rome, Italy, (*Vice-Chairman*)

Sir Horace Smirk, Professor of Medicine, University of Otago Medical School, Dunedin, C.I., New Zealand, (*Chairman*)

Dr C. Wilson, Professor of Medicine, University of London ; Director, Medical Unit, The London Hospital, London, E. 1, England (*Rapporteur*)

Secretariat :

Dr Z. Fejfar, Chief, Cardiovascular Diseases, WHO (*Secretary*)

ARTERIAL HYPERTENSION AND ISCHAEMIC HEART DISEASE

PREVENTIVE ASPECTS

Report of an Expert Committee

The WHO Expert Committee on Arterial Hypertension and Ischaemic Heart Disease met in Geneva, Switzerland, from 16 to 23 October 1961.

The meeting was opened by Dr F. Grundy, Assistant Director-General of WHO. Sir Horace Smirk was elected Chairman, Dr V. Puddu, Vice-Chairman, and Dr C. Wilson, Rapporteur.

1. INTRODUCTION

The Expert Committee on Cardiovascular Diseases and Hypertension which met in Geneva in October 1958 gave special consideration to the classification and criteria for diagnosis of hypertension and coronary artery disease. The report of this Committee,¹ published in 1959, provided a basis for planning comparable epidemiological studies.

The present Committee was asked to consider the prevention and control of these diseases. It was thought logical to constitute this Committee largely of clinicians who could provide public health authorities with the clinical basis for preventive measures. It is important that epidemiologists working among population groups, and clinicians investigating the natural history of disease in individuals, should have a unity of purpose in applying scientific methods of study.

The primary objectives of the present Committee were to summarize the present state of knowledge, sifting out facts from impressions, in order to put forward proposals for health protection and medical care which might prevent the occurrence, or the progression, of arterial hypertension and ischaemic heart disease. In addition, the Committee was asked to indicate fields in which research was particularly necessary for this purpose.

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

2. PREVENTION AND CONTROL OF ARTERIAL HYPERTENSION

2.1 Terminology and classification

The term arterial hypertension is used to indicate a rise in arterial blood pressure, and in the great majority of cases both systolic and diastolic pressures are elevated. Some cases—a minority—are due to recognizable causes such as renal disease, endocrine disease, coarctation of the aorta, or toxæmia of pregnancy. However, in the great majority of patients with elevated blood pressure, no such cause is found and the term essential hypertension has been applied to this group. Essential hypertension is defined, therefore, as high blood pressure without apparent primary organic cause.¹ In the elderly, systolic blood pressure may be raised while diastolic pressure is normal or only slightly elevated. Such cases should probably be separated from the main group of essential hypertension, as the increased blood pressure probably represents a response to increased rigidity of the larger arteries. When arterial hypertension runs an accelerated course, leading in particular to severe renal and retinal lesions including papilloedema, the term malignant hypertension is used.

2.2 Methodology of blood pressure determination

The Committee re-affirms the methodology specified in the report of the Expert Committee on Cardiovascular Diseases and Hypertension² with the following additional comment.

2.2.1 *Type of apparatus to be used*

There is evidence that a more objective "blind" technique may minimize some types of inter-observer variation and may, therefore, be superior to standard sphygmomanometry for population studies where comparability is important. Continuous automatic recording devices, using either indirect or intra-arterial methods, are desirable for some investigations. A mercurial manometer, or properly calibrated aneroid instrument, remains, however, the basic equipment for common use. The recommendation made by the Expert Committee on Cardiovascular Diseases and Hypertension that cuffs 14 cm in width should be used, with

¹ In some countries the term "hypertensive disease" is used where this report uses the term "essential hypertension". In other countries, however, "hypertensive disease" is used as a general term to cover all forms of high blood pressure.

² *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

inflatable bags of sufficient length to surround the arm, has not yet been generally accepted. Evidence continues to accumulate in support of these precautions.

2.2.2 *Measurement of systolic and diastolic pressures*

The instrument should be placed on a level surface if a mercurial manometer is used. The cuff is applied evenly and firmly to either arm, removing sufficient clothing to give adequate exposure. The lower edge of the cuff should be about 2 cm above the antecubital space with the rubber bag centred over the course of the brachial artery. The uninflated cuff should not compress the underlying tissue. The cuff is rapidly inflated to a point 20-30 mm Hg above the pressure at which the radial pulse is obliterated. The stethoscope is applied immediately below the edge of the cuff over the area where the brachial artery pulse is palpable. Cuff pressure is then permitted to fall at a rate of not more than 2-3 mm Hg per pulse-beat, and the point of first appearance of an audible pulse-beat is recorded as the systolic pressure. The cuff pressure is permitted to fall further and the sounds will commonly be noted to become quite suddenly muffled (phase 4) and shortly to disappear (phase 5). Until it becomes clear which phase more correctly represents the diastolic value, both pressures should be recorded.

2.2.3 *Casual blood pressure determination*

For "casual" blood pressure determination no definite preparation of the subject is specified. However, careful attention should be paid to the elimination of factors which might affect the reading. Noise, chilling and emotional stimuli should be minimized. The position of the subject should be the same for all determinations, and the sitting position is recommended for comparative purposes even when measurements in other positions are required. If hypotensive drug therapy is being studied, pressures should be obtained with the patient in the recumbent position and after standing for at least one minute. A record of the pulse-rate at the time of blood pressure determination provides a useful indication of the state of the subject.

The observer should have adequate training and experience, and it is important that his hearing should be normal.

2.2.4 *"Basal" and "near-basal" blood pressure*

It has been suggested that by taking special precautions over blood pressure determination the disturbing effect of environmental factors can be avoided, so that pressures are obtained which are considerably lower than the casual value. When very strict precautions are taken, the term

“ basal ” blood pressure has been applied ; with less stringent precautions, “ near-basal ” has been used. The difference between the basal and casual values has been termed “ supplemental ” pressure. While the Committee expresses no view on the absolute significance of the basal level or the consistency with which it may be obtained, it feels nevertheless that a standardized technique to eliminate disturbing environmental factors may be of considerable value. It has therefore been felt justifiable to describe one possible technique for such determinations.

When taking the “ basal ” blood pressure an attempt is made to ensure that the subject is in a state of minimal physical, mental and metabolic activity, comparable to conditions under which basal metabolic rate is measured. A room is set aside for the determination, free from any outside disturbance, and the subject is reassured and encouraged to relax. The determination is made at home or in hospital, with the subject in the fasting state, after a satisfactory night's sleep and if necessary after the bowels and bladder have been emptied. Blood pressures are taken by a trained technician at not less than half-minute intervals for 15 minutes, and the average of the two lowest readings is taken as basal. The pulse-rate is recorded at the same time. More reliable results are obtained if a sedative is used, but this may be omitted if the patient usually sleeps well.

“ Near-basal ” blood pressure is measured by the same technique without overnight stay in hospital, and such determinations may be made at any time of the day but preferably in the morning.

2.3 Diagnosis

In considering preventive and therapeutic measures in arterial hypertension, diagnosis is of primary importance since the results of therapy depend on the nature of the underlying disease. Recent methods of investigation have revealed that some cases previously diagnosed as essential hypertension may be of renal or endocrine origin. Nevertheless, there is good reason to suppose that these represent only a minority of cases in this large group. The actual diagnostic measures to be applied depend on the character of the project and are discussed later (see page 17).

Examination of the urine for protein should always be made. This will exclude most patients with renal disease, but relatively few patients in the group of essential hypertension. A detailed account of the differential diagnosis of renal hypertension in its various forms and of essential hypertension is given in Annex 2 (see page 27).

2.4 Stages of essential hypertension

In a previous report¹ essential hypertension was divided into “ complicated ” and “ uncomplicated ”. In the view of the present Committee a classification of the disease which takes into account the *stages* of its

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

natural history would appear to be more useful. It is therefore proposed that essential hypertension should be classified as follows :

- Stage 1* High blood pressure without evidence of organic changes in the cardiovascular system.
- Stage 2* High blood pressure with cardiovascular hypertrophy but without other evidence of organ damage.
- Stage 3* High blood pressure with evidence of organ damage attributable to the hypertensive disease.

It is obvious that such a grading may be applied not only to essential hypertension but to all forms of arterial hypertension.

In the description which follows, an attempt has been made to include the main diagnostic signs which will help the clinician to place the patient with some assurance in the appropriate stage of the disease. Nevertheless, it is not always possible to separate clearly one stage from another. This is due in the first place to uncertainties which arise from present methods of diagnosis, and it may be hoped that some of these will be resolved by further study; in the second place there may be difficulty in interpreting the relationship of certain symptoms, such as headache and dyspnoea, to the stages of the disease. It must be emphasized, moreover, that this sequence of stages may not necessarily develop in all patients with high casual blood pressure.

2.4.1 *Identification of stages*

Stage 1. There are at this stage no objective signs in the cardiovascular system of organic changes produced by hypertension. Nevertheless symptoms may be present which may be related to anxiety, but in some cases appear to be attributable to the raised blood pressure level.

The Committee was in full agreement with the conclusions of the previous report¹ that there is no sharp line of demarcation between normotensive and hypertensive levels—i.e., it is not possible in the individual to give an absolute figure for the upper limit of normal blood pressure by which Stage 1 may be identified. Nevertheless, for screening purposes in population groups certain values may be accepted, using "casual" blood pressure recording: (1) below 140/90 mm Hg—normal range; (2) 160/95 mm Hg and above—hypertensive range.

Certain qualifications have to be made for age and sex. Thus the figure of 160/95 is acceptable as the upper limit of normal below the age of 60 but may not be acceptable in elderly subjects, in whom elevation of systolic pressure may reflect increased rigidity of the large arteries. In younger subjects, e.g., 30-40 years of age, figures between 140/90 and

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

160/95 would, in many cases, be regarded with suspicion, and such individuals might well be kept under observation. In women, a less serious prognosis is attached to the same high level than in men.

Stage 2. Identification of this stage is based on the objective signs of cardiovascular hypertrophy.

The presence of *left ventricular hypertrophy* may be established by (1) physical examination, (2) radiography, and (3) electrocardiography.

(1) *Physical examination*

The chief clinical sign of left ventricular hypertrophy is a heaving apex beat, especially if this is displaced downwards. There is considerable variation between different observers in evaluating this sign, so that other methods of investigation are usually necessary to establish the presence of left ventricular hypertrophy.

(2) *Radiological findings*

The heart may appear normal in the radiograph even when left ventricular hypertrophy is considerable. A relative lengthening and increased convexity of the left lower border in the postero-anterior position is strongly suggestive. Marked enlargement of the heart indicates that dilatation is present as well as hypertrophy, and such patients should properly be placed in Stage 3.

(3) *Electrocardiogram*

The electrocardiogram provides the most reliable indication of left ventricular hypertrophy. At present there is no generally applicable set of criteria. Unfortunately, too many criteria have been employed in the diagnosis and it has become clear that any one of these which is highly sensitive tends to produce false positive results. It is probable that in the near future improved techniques will lead to revision of current concepts.

With these reservations high-voltage criteria, as described by Sokolow & Lyon¹ (RV_5 or $RV_6 + SV_1 = 35$ mm or more) provide a reasonably clear basis for a provisional diagnosis of left ventricular hypertrophy in the adult. If these voltage criteria are extended to peripheral leads, or if ST segment and T wave changes of the "hypertrophy" type are included, specificity is increased.

Vascular hypertrophy. Information on the state of the arteries may be obtained from examination of the peripheral vessels and the optic fundi. The radial and brachial arteries should be palpated, although the

¹ Sokolow, M. & Lyon, T. (1949) *Amer. Heart J.*, 37, 161.

presence of vessel wall hypertrophy may be difficult to assess. More reliable information can be obtained from examination of the retinal arteries. Tortuosity and arteriovenous compression are typical of Stage 2. The Committee strongly recommends that examination of the fundi should be carried out by the physician himself, and that students should be trained to examine and evaluate retinal changes in patients with hypertension. Wherever possible retinal photography should be used to obtain an objective record. A hand camera using 35-mm film (black and white or coloured) is now available.

Stage 3. In this stage, symptoms and signs result from damage in various organs due to the hypertensive process or secondary vascular lesions.

(1) *Heart* : Characteristic of this stage are the signs and symptoms of heart failure, or manifestations of ischaemic heart disease consequent on accelerated atherosclerotic changes in the coronary arteries. Physical examination may reveal displacement of the apex beat outside the midclavicular line due to cardiac dilatation, and this will be confirmed by marked widening of the heart shadow in the postero-anterior and left anterior oblique views. Pulmonary congestion leads to increasing dyspnoea on exertion, although breathlessness as an isolated symptom is not sufficient to classify the patient in Stage 3. Paroxysmal nocturnal dyspnoea and other signs of heart failure may develop, and there may be radiographic evidence of pulmonary congestion.

(2) *Brain* : Cerebrovascular accidents are manifested by signs of persistent brain damage. Transient attacks of paralysis, or sensory disturbance, or hypertensive encephalopathy may occur, and may be followed by persistent signs of organic vascular lesions. (The term hypertensive encephalopathy is used to indicate sudden and reversible attacks in which headache, blindness, disorientation, convulsions and coma may occur.)

(3) *Ocular fundi* : The appearance of exudates, retinal oedema, haemorrhages and vascular thrombosis are unequivocal signs of Stage 3 arterial hypertension. The additional finding of bilateral papilloedema indicates the development of the malignant course.

(4) *Kidney* : Difficulties may arise in distinguishing renal damage due to essential hypertension from primary renal disease. These problems are dealt with in Annex 2 (see page 27). In the malignant phase, renal involvement is almost invariable and progresses rapidly. In other cases of essential hypertension renal damage is not usually severe enough to give rise to symptoms; nevertheless, proteinuria and impairment of renal function may be indicated by laboratory tests, particularly when the high blood pressure is long-standing.

2.5 Renal hypertension

Renal hypertension may be due to chronic pyelonephritis, diabetic glomerulosclerosis, glomerulonephritis, renal artery stenosis and a variety of other rare diseases of the kidneys. The frequency with which these conditions cause hypertension in different communities is unknown but in most this is almost certainly low compared with essential hypertension. In a number of centres, chronic pyelonephritis has been found at autopsy in 2% to 6% of post mortems, but the disease is frequently undiagnosed during life. With the improved means at our disposal this may now be remedied (see Annex 2, page 27). There is both experimental and clinical evidence that pyelonephritis may complicate other forms of renal disease, and this must be taken into account in assessing the importance of primary urinary tract infection as a cause of hypertension. Recent work has drawn attention to the fact that unilateral renal artery stenosis may give rise to hypertension which closely resembles essential hypertension, in that renal involvement is slight and indeed may only be detected by special methods of investigation. The frequency with which this condition acts as a primary cause of hypertension is difficult to establish, since atheromatous occlusion of the renal arteries may occur as a complication of essential hypertension. Further investigation, both clinical and pathological, is needed to clarify this point.

High blood pressure occurs in the majority of cases of chronic kidney disease, and malignant hypertension develops in a far greater proportion of such cases than in patients with essential hypertension. In general, the blood pressure rises late in the course of the renal disease, usually when renal function is moderately and irreversibly impaired. The hypertension often progresses rapidly through the stages we have described for essential hypertension; hence treatment is important to prevent aggravation of the renal damage. Such treatment should be carried out with caution when renal function is severely reduced.

2.5.1 *Other forms of arterial hypertension*

High blood pressure due to other rather rare conditions such as endocrine disease and coarctation of the aorta may be detected in screening, and these patients should be submitted to a more detailed examination. Further discussion from the point of view of preventive treatment does not appear to be necessary.

2.6 Preventive and therapeutic measures

The aim of prevention is in the first place to minimize the occurrence of high blood pressure, and in the second place, to prevent further progres-

sion leading to the later ill-effects. In view of our lack of knowledge of etiological factors, no effective measures can at present be recommended which will prevent the occurrence of essential hypertension, nor can susceptibles yet be identified. Action is therefore limited to therapeutic remedies directed against the progressive effects of the disease. In renal hypertension, some steps can be taken to prevent the development of the primary disease—e.g., chronic pyelonephritis.

2.6.1 *Clinical aspects*

2.6.1.1 *Essential hypertension*

The problems of preventive therapy, as defined above, will first be discussed in relation to the three stages of essential hypertension.

Stage 1. The Committee feels that different factors may contribute to the hypertension at this stage. Thus in some patients nervous or emotional stress appears to be of major importance. There is evidence that in such cases change of environment may lead to a fall in the blood pressure level, and to the relief of associated symptoms. A return to the stressful environment is, however, often associated with reappearance of hypertension. The role of environmental stress may vary in different age-groups. It is generally agreed, therefore, that what may be described as "common-sense psychotherapy" is the most effective treatment, possibly combined with a change in environment where symptoms are referable to anxiety. Apart from sedation, treatment with drugs is usually unnecessary and ineffective.

There is inadequate evidence on the natural history of the disease in this stage, and more information is required on its prognosis and the factors which may determine transition to the later stages. Furthermore we do not know whether treatment of the hypertension in Stage 1 can prevent the development of Stage 2. Such evidence will be difficult to obtain since treatment would need to be continued for a very long period before a satisfactory conclusion could be reached. Well-controlled studies should be undertaken, however, with a view to clarifying the natural history of this common form of hypertension.

Stage 2. The detection of subjects with Stage 2 essential hypertension is particularly important since effective therapy may delay or avoid the severe developments of Stage 3. Thus congestive heart failure can be prevented, and there is evidence that the risk of malignant hypertension is reduced. Whether cerebral vascular accidents can be prevented is a more controversial question, but there are some reports that their incidence may be diminished. Regular supervision and follow-up of all subjects in this stage are necessary. Attention should be paid to environmental factors,

although more reliable information is needed on the importance of these. Thus removal from stressful occupations, weight reduction, and low salt intake have all been recommended, although there is no certain evidence of their specific value. Drug therapy is the most effective measure at this stage. Nevertheless physicians should be cautioned against the routine use of hypotensive drugs on all patients with elevation of the casual blood pressure. It cannot be too strongly emphasized that treatment is an individual matter for each patient. Once treatment is instituted, continuous and adequate supervision is essential to maintain satisfactory control.

Stage 3. It is obvious that patients discovered in Stage 3 of essential hypertension must be considered for treatment with hypotensive drugs. In the treatment of heart failure, for example, these drugs can be extremely effective. Careful selection is necessary since the presence of certain complications may contra-indicate sudden or severe lowering of the blood pressure. Apart from the urgent treatment of acute complications, such as heart failure and encephalopathy, blood pressure reduction should be carried out with caution in patients with severe ischaemic heart disease, renal damage or cerebrovascular disease.

2.6.1.2 *Renal hypertension*

Preventive measures against the *occurrence* of renal hypertension must be directed to the prophylaxis of the various renal disorders. There is a need for the promotion of such measures in pyelonephritis, and recent evidence indicates that the infection is preventable in many cases. The infecting organisms are frequently introduced into the urinary tract by catheterization, and this procedure should not be used to obtain clean urine specimens for diagnosis. Quantitative bacterial counts on the urine indicate that ascending pyelonephritis frequently develops in patients with asymptomatic bacilluria, for example during pregnancy, and effective treatment of the bacilluria may prevent the development of pyelonephritis. More thorough and prolonged antibacterial therapy in acute pyelitis will prevent many cases from progressing to the chronic stage.

Preventive measures in glomerulonephritis are more difficult, but the treatment of streptococcal infection, especially when this occurs in epidemics, diminishes the risk of occurrence of glomerulonephritis. There is good evidence that its incidence has decreased in recent years with the more effective treatment of streptococcal infection.

Unilateral renal disease, although a comparatively rare cause of renal hypertension, is important since, in young subjects particularly, removal of the damaged kidney may restore the blood pressure to normal. Renal artery stenosis is a special form in which, according to present evidence, arterial surgery without nephrectomy may produce beneficial results.

2.6.2 *Public health aspects*

The application of the measures indicated above on a public health basis can now be considered, although it is clear from what has already been said that preventive action is feasible only on a limited scale at present.

2.6.2.1 *Surveys*

Using the classification of arterial hypertension into stages, as already defined, surveys may be undertaken with the aim of determining the characteristics and extent of the problem, as well as for instituting preventive treatment.

A basic factor in all epidemiological studies is the validity of the casual blood pressure determination. A standard method for taking blood pressure is necessary, and this has already been discussed with reference to casual, basal and near-basal pressures. The techniques used will depend on the nature of the project, and there is an obvious need for further studies to determine the most valid method of blood pressure estimation in relation to subsequent morbidity. This would be of value both to clinical practice and to epidemiological research. From what has already been said, other criteria should be included for purposes of classification and diagnosis. Thus examination of the urine for protein and sugar should be a part of screening, and the discovery of hypertension should be followed by appropriate examination for cardiovascular hypertrophy and signs of organ damage in order to determine the stage of the disease.

Various population groups can be screened to obtain information on prevalence—for example, office workers and factory workers. Age limits may be restricted to between 20 and 60 years. Certain individuals may deserve particular attention because of their possible predisposition to hypertension—for example, those with a family history of high blood pressure or its complications, or diabetes, and those engaged in occupations involving considerable nervous stress.

Blood pressure determination should be included in routine medical examination for employment and military service, and might well be incorporated in mass detection programmes for such diseases as tuberculosis, cancer and syphilis.

Screening programmes should not be undertaken unless full facilities are available for further investigation and for treatment where necessary of those found to have high blood pressure. Moreover, there are few diseases in which there is a greater risk of anxiety symptoms developing from awareness of the diagnosis and its possible consequences. Whilst we are in no doubt about the gravity of the problem of arterial hypertension, and the need for its further investigation and control, a primary

object of any public health undertaking must be the prevention of further invalidism due to these activities. It cannot be too strongly emphasized that individuals should not be informed of the finding of high blood pressure unless this is necessary for treatment and unless effective therapy can be given.

2.6.2.2 Training of professional and technical personnel

Parallel with this is the need for a training programme for physicians and technical workers, to familiarize them with the techniques of blood pressure determination and the continually changing problems of therapy.

Treatment with hypotensive drugs gives rise to many problems, particularly for the family doctor. The multiplicity of drugs administered, the need for frequent adjustments of dosage, the troublesome nature of side effects, all emphasize the need for regular medical consultation and supervision. This could be most effectively carried out in collaboration with specially equipped clinics provided with fully qualified staff experienced in the management of the disease, trained technicians, and facilities for record-keeping. Under these circumstances, long-term observations could provide information on the clinical, epidemiological and therapeutic problems already mentioned.

2.6.2.3 Health education

Since the present treatment and possible lines of prevention of cardiovascular disease may involve considerable alteration in the way of life of individuals, it is important that the public should be informed about the nature of the problem. To ensure that health education is appropriate, studies should be made of current popular ideas regarding cardiovascular diseases, their natural history, and their supposed etiological factors. There is a danger that ill-conceived health education may cause unnecessary anxiety and even result in unwillingness of patients to declare their symptoms. As in other medical problems where the etiology is obscure, but where early detection followed by appropriate treatment may prevent progression of the disease, the main aim of public health action should be to persuade people to present themselves for examination during the period of risk. Where the objective is to study etiology or prevention, education should encourage the public to provide the necessary co-operation.

2.7 Research aspects

In the light of the foregoing discussion, the Committee consider that the following aspects of hypertensive disease are in special need of further investigation.

2.7.1 *Methodology and diagnosis*

The development of apparatus for automatic recording of blood pressure. Comparison of direct and indirect methods for diastolic pressure measurement at phase 4 (muffling) and phase 5 (disappearance of sound).

The interrelations of casual, basal and supplemental blood pressures, and factors which affect these.

Techniques for the more accurate diagnosis of left ventricular hypertrophy and dilatation, e.g., measurement of heart volume; electronic timing in radiography; computer techniques in electrocardiography.

Improvements in the diagnosis of renal artery stenosis, and studies of the frequency with which this condition causes hypertension.

Studies on the early detection of bacteriuria. Investigation of pyelonephritis in countries where its prevalence is high, particularly in relation to hypertension.

The use of questionnaires and their adaptation for different populations and countries.

Inquiry into the validity of certified causes of death with reference to analysis of vital statistics.

2.7.2 *Natural history of the disease*

Investigation of the course and prognosis of essential hypertension in its early stages, and in different age-groups.

The relationship of basal and supplemental blood pressures to the reversibility of hypertension and to the development of cardiovascular hypertrophy.

2.7.3 *Etiology*

Investigation of the genetic factor in essential hypertension. Studies in twins.

Relationship of hypertension to occupational stress. The Committee draws attention once again to the need for expert consideration of methodology in the investigation of nervous stress in relation to cardiovascular disease.

Studies of hypertension in relation to urbanization and industrialization of population groups. There is a need for the co-ordination of parallel studies in different countries, and especially for standardization of techniques.

Haemodynamic studies of essential hypertension in man and of experimental hypertension in animals.

2.7.4 *Therapy*

Long-term studies on the effects of treatment in the various stages of arterial hypertension.

Continuing research for more effective therapeutic agents which are free from the side effects and other disadvantages of those at present available.

2.7.5 Classification

The Committee was informed of the preparations for revision of the International Statistical Classification of Diseases, Injuries, and Causes of Death. At present arterial hypertension is not coded as a cause of death when it is complicated by vascular disease, e.g., ischaemic heart disease or cerebral vascular disease. The Committee strongly recommends that this omission should be rectified. Arterial hypertension should be mentioned on the death certificate whenever it is known to be present, and the revised Classification should make it possible to record the association of vascular lesions in various organs with high blood pressure.

3. PREVENTION AND CONTROL OF ISCHAEMIC HEART DISEASE

3.1 Terminology and classification

The term "ischaemic heart disease" was defined by the World Health Organization's Study Group on Atherosclerosis and Ischaemic Heart Disease¹ as "the cardiac disability, acute and chronic, arising from reduction or arrest of blood supply to the myocardium in association with disease processes in the coronary arterial system". The Expert Committee on Cardiovascular Diseases and Hypertension² accepted the term "coronary heart disease" as synonymous with ischaemic heart disease as defined above.

The present Committee would only point out that ischaemic heart disease is not synonymous with atherosclerotic heart disease, since it may be the result of certain other pathological processes of the coronary arteries. Atherosclerosis is, however, by far the most frequent cause and the most important from the point of view of public health measures of prevention and control. The present report will be confined therefore to the problems of atherosclerotic heart disease.

The classification of ischaemic heart disease into angina pectoris and myocardial infarction is inadequate from a clinical point of view for purposes of prevention and control, since it does not include (a) intermediate cases between angina of effort and myocardial infarction, (b) cases with chronic

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1957, 117.

² *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

heart failure and other manifestations such as arrhythmia and heart block, commonly attributed to atherosclerotic heart disease, (c) cases of sudden death. For these reasons, we suggest that for the purposes of this enquiry ischaemic heart disease should be sub-divided as follows :

- (1) Angina effort
- (2) Myocardial infarction (old and recent)
- (3) Intermediate types
- (4) Ischaemic heart disease without pain
 - (a) Asymptomatic
 - (b) Non-specific effects of chronic myocardial damage. This group includes cases with chronic heart failure and other manifestations such as arrhythmia, attributable to atherosclerosis.

This classification now covers all patients with ischaemic heart disease in whom sudden death may occur.

3.2 Diagnostic criteria

3.2.1 Angina of effort

In this group are placed individuals with pain or discomfort localized in the upper or mid-sternal region and appearing during effort, especially on walking or starting to walk. The pain may remain localized in the chest, radiate within the chest, or radiate to the shoulders, arms or jaws, on one or both sides. It is crushing or constricting in character, occasionally numb or burning, and compels the patient to stop or slow down. After the cessation of effort or the use of sublingual nitroglycerine, the pain disappears in one or two minutes in most cases, but the interval may be of shorter or longer duration. In cold surroundings, after eating, or when walking uphill or into the wind, pain is more easily produced. It may begin or remain localized in any one of the above radiation sites. Pains which appear during emotional crises, especially anger, at the moment of lying down, or during sexual intercourse have the same significance as those occurring on effort. The diagnosis of angina of effort may be made on the above criteria even in the absence of electrocardiographic changes.

3.2.2 Myocardial infarction

3.2.2.1 Recent myocardial infarction

Recent (or acute) myocardial infarction is recognized in typical cases by the occurrence of anginal pain with the following characteristics :

- (1) Diffusion through the chest, anteriorly or generally, or to the points of radiation described under angina of effort.

- (2) Extreme, at times agonizing, intensity.
- (3) Resistance to nitroglycerine.
- (4) Long duration, usually several hours.

It may be associated with other disturbances such as dyspnoea with a sense of suffocation, "indigestion", general malaise and sweating. An initial fall in blood pressure, which may reach shock levels, and, later, rise in temperature, are confirmatory signs. Cases with atypical symptomatology not infrequently occur.

Evidence of muscle necrosis will be obtained by laboratory investigations, including leucocyte count, sedimentation rate and changes in specific enzyme activity. The electrocardiogram will show a variety of abnormal patterns due to necrosis; these are more clearly diagnostic if serial changes can be demonstrated.

3.2.2.2 *Old myocardial infarction*

In this group are placed individuals with a clearly documented history of previous acute infarction. The presence of cardiac aneurysm, although rare, is also acceptable evidence. The diagnosis may also be made with reasonable certainty if the electrocardiogram shows typical pathological coronary Q waves.

The Committee has refrained from giving a detailed description of electrocardiographic patterns in the above categories of ischaemic heart disease. A full account of these was given in the report of the Expert Committee on Cardiovascular Diseases and Hypertension.¹ This undoubtedly requires revision in the light of further experience. In the near future the development of new techniques may bring about further changes in interpretation. This matter is, at present, under study.

3.2.3 *Intermediate types*

There are various syndromes, poorly classified at present, which represent more than angina of effort, for instance angina pectoris occurring at rest or of long duration, but in which nevertheless evidence of myocardial necrosis is lacking. The Committee does not feel that a more useful definition and classification of this group can be made at present.

3.2.4 *Ischaemic heart disease without pain*

3.2.4.1 *Asymptomatic*

To this category are assigned those who show strongly suggestive electrocardiographic signs of ischaemic heart disease in the absence of

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

symptoms. The changes in ST segments and T waves, usually classified as "ischaemic", are sufficiently significant if they are produced after exercise or are accompanied by evidence of atherosclerosis outside the heart.

3.2.4.2 *Non-specific effects of chronic myocardial damage*

Cases in this category show various manifestations of chronic myocardial damage, particularly chronic heart failure, auricular fibrillation and heart block. The diagnosis, which can be presumptive only, depends on excluding other forms of heart disease and detecting the presence of atherosclerotic changes outside the heart.

3.3 Preventive and therapeutic measures

The possibility of applying preventive measures in ischaemic heart disease is at present limited by the incompleteness of our understanding of etiology, and difficulties in early diagnosis. Recent evidence has suggested strong associations between ischaemic heart disease and certain factors such as high blood cholesterol and hypertension, but at almost all points further information is needed before these relationships can be given practical application.

3.3.1 *Screening and case-finding*

There are two distinct problems in population surveys, namely, the detection of individuals who may be predisposed to ischaemic heart disease, and those in whom the disease has developed. It must be pointed out that preventive measures apply equally to both groups, particularly to those who have already shown signs of the disease and who may suffer from recurrence at intervals of many years. Coronary atherosclerosis is much more widespread than clinically recognizable ischaemic heart disease, so that, in addition to the clinical signs and before these have appeared, it is necessary to take into account certain factors which may indicate that the subject is exposed to increased risk. These include high blood pressure, high serum cholesterol, obesity, diabetes, heavy cigarette smoking, and a family history of relevant cardiovascular disorders. A complex screening technique is required to detect all these factors, and such a technique may be inapplicable to large populations. For this reason selective screening of particular "vulnerable" groups must be made, for example with reference to age, sex and occupation. Middle-aged men in sedentary occupations are worthy of special attention.

The use of blood lipid levels as a criterion of increased risk of ischaemic heart disease presents considerable difficulties. There is evidence that a relationship exists between a high blood lipid concentration and atheroma

formation, but there is at present no convincing evidence that individual blood lipid fractions have a specific action. In practice, however, it is believed that the cholesterol level may be accepted as an index of susceptibility to ischaemic heart disease. In using this as a screening criterion for preventive measures, it is necessary to decide on a level above which individuals should be selected for treatment. It cannot be assumed, however, that the mean level for any age-group of the population represents a "normal" figure in the sense that individuals at or below this level are not at risk. Thus the selection of any particular cholesterol level for prophylactic trials is purely arbitrary.

Atherogenesis is a complex problem involving abnormalities in the vessel wall, intravascular thrombosis, and thrombolytic activity. The blood lipid level is only one factor, although probably an important one, relating to these various phenomena. In planning preventive measures, therefore, screening procedures must take into account other factors, including inheritance, hypertension, physical activity, nervous stress, occupation and endocrine function.

The following is a screening procedure which, in the light of present knowledge, covers the basic requirements. From this a selection may be made according to the special circumstances and facilities available.

3.3.1.1 *History*

Data as to age, sex, occupation, family background, smoking habits, ethnic origin; angina of effort; previous symptoms, particularly evidence of past myocardial infarction. A suitably designed questionnaire may considerably increase the accuracy of diagnosis of angina pectoris.

3.3.1.2 *Physical examination*

Complete general examination with special reference to blood pressure, height, weight, skin-fold measurements; evidence of predisposing diseases; detection of other cardiovascular disorders.

3.3.1.3 *Laboratory examinations*

Electrocardiogram; exercise tolerance tests (under medical supervision) in symptomatic cases where the electrocardiogram at rest shows no evidence of ischaemia; serum cholesterol measurement; urinalysis for sugar and protein.

3.3.2 *Preventive measures*

It must be repeated that at the present time there are no effective means by which the occurrence of ischaemic heart disease can be prevented. Such therapeutic measures as are available must therefore be applied to

the disease itself in the hope of delaying its progression or preventing late complications.

3.3.2.1 *Dietary control in relation to blood lipid factors*

It is accepted that most animal fats tend to increase blood cholesterol and might therefore be regarded as atherogenic, whereas most vegetable fats do not have this effect. Nevertheless, much further research is needed before public health authorities can recommend major alterations in the diet, or are justified in advising that more or less of any particular kind of fat would be beneficial. So far, evidence is lacking that reduction of blood cholesterol, by dietary or other means, reduces the incidence of further episodes in patients with established ischaemic heart disease. It would appear desirable, therefore, to attack the problem at an earlier stage in an attempt at prevention in individuals who are predisposed, but do not yet suffer from the disease. There are very considerable difficulties in carrying out such a preventive dietary trial, since it should start at an early age, before atheroma is presumed to be established, and must continue for a long period of time before the effects of prevention becomes manifest. We have referred also to the problem of the population sample to be screened, the size of which would depend on the criteria of selection and the local circumstances and facilities available.

The question of obesity may properly be dealt with at this point. There is evidence that obesity is associated with an increased susceptibility to ischaemic heart disease; this is, however, only true in association with other factors, which include hypercholesterolaemia and hypertension. There is so far no clear-cut evidence that obesity alone has any specific bearing on the problem of atherosclerosis. Obesity is in general due to over-eating, which for obvious reasons should be discouraged. Apart from this, dietary restrictions, either in relation to fat content or total calories, must be related to the individual's requirements with reference to the physical nature of his occupation, state of nutrition, and level of metabolism.

3.3.2.2 *Other factors affecting blood cholesterol level*

It is known that certain hormones and vitamins may lower the blood cholesterol level, but administration of these substances in effective doses is outside the realm of large-scale therapy, and there is so far no evidence that this might have a beneficial effect on the occurrence or progress of ischaemic heart disease.

A number of drugs which interfere with cholesterol synthesis have recently been introduced. Here again there is so far no evidence of a preventive effect on the occurrence of atherosclerosis or its complications,

so that the use of such substances must be regarded as strictly a subject for further investigation.

3.3.2.3 *Adjustment of habits and way of life*

The Committee carefully examined available evidence on the role of physical activity, nervous stress, and smoking in the pathogenesis of ischaemic heart disease. Although these factors may be of importance, the available information does not justify any definite recommendation. Further information is needed on these problems.

3.3.2.4 *Treatment of hypertension*

Since high blood pressure has been clearly shown to accelerate the development of atherosclerosis, it is rational to include the treatment of hypertension in the prevention of ischaemic heart disease. The methods, indications and precautions have been discussed previously in this report (see page 11).

3.3.2.5 *Anti-coagulant therapy*

There seems to be little disagreement about the usefulness of anti-coagulant therapy in preventing thromboembolic complications or further thrombosis during the first two months after an acute attack of myocardial infarction, providing that the known contra-indications are respected, adequate control is available, and withdrawal of therapy at the end of this period is gradual. Moreover, evidence from various sources strongly suggests that after a first myocardial infarct in patients under 60 years of age, anti-coagulant therapy reduces the risk of recurrence during the first year. In the broad group of patients with angina it does not appear justifiable to make any general recommendation until further information is available, but there is preliminary evidence that during the first two years after the onset, anti-coagulant therapy reduces the risk of infarction. There is no evidence at present that anti-coagulant therapy is beneficial in asymptomatic ischaemic heart disease or in subjects predisposed to the disease but not suffering from it.

In avoiding the haemorrhagic complications of anti-coagulant therapy, a well-planned organization with good laboratory facilities, together with careful selection and supervision of patients, provide the best protection. Under these conditions mortality attributable to this therapy is less than 0.5% per annum. Particular precautions should be taken in cases with arterial hypertension, or with a history of peptic ulcer or cerebrovascular accident. These conditions, lack of co-operation from the patient, or inadequate facilities for control of dosage, may indeed contra-indicate anti-coagulant therapy.

3.3.2.6 *Other public health activities*

In ischaemic heart disease, the same general principles apply as were described for arterial hypertension, particularly in relation to health education of the public and instruction of professional and technical workers. Here also screening can be included in mass detection programmes for other diseases, and the precaution is equally necessary that screening should be carried out only when adequate facilities are available for medical supervision and treatment. The complexity of both diagnosis and treatment underlines the need for small-scale surveys, and the purposes to which these can be applied are indicated later under research aspects.

Many of these projects involve epidemiological studies and facilities for these should be expanded. Co-operation with other research groups in cardiovascular diseases is most desirable at all stages.

There are certain specific measures which particularly apply to ischaemic heart disease. Of great importance is the provision of facilities for the emergency treatment of cardiac arrest and the practical instruction therein of medical staff and students. This subject should be included in the training of postgraduates and in refresher courses for general practitioners.

Special arrangements are necessary for the rehabilitation and re-employment of patients with ischaemic heart disease, including suitable restriction of working hours and adequate rest leave.

3.4 **Research aspects**

3.4.1 *Methodology and diagnosis*

Further studies on the early diagnosis of ischaemic heart disease.

The study of intermediate and atypical forms in relation to the accepted manifestations of ischaemic heart disease.

Investigation of validity of death certification as recommended for arterial hypertension (see page 15).

Standardization of blood lipid analysis.

Electronic data-processing techniques for electrocardiographic diagnosis and epidemiological surveys.

3.4.2 *Etiology*

Further studies into the influence of environmental factors and their inter-relations in pathogenesis—e.g., diet, smoking, physical exercise, occupation, and nervous stress.

Genetic studies in relation to blood lipid levels and predisposition to atherosclerosis.

Studies of comparative incidence of coronary thrombosis and hypertension, particularly in relationship to developing communities with increasing urbanization.

Surveys of the morbid anatomy of atherosclerosis in different communities.

Studies of vital statistics in order to elucidate trends in mortality in relation to associated diseases, especially hypertensive disease.

Experimental studies on the production of atherosclerosis in animals.

Relationship of endogenous metabolic disorders to ischaemic heart disease.

Studies on the metabolism of the arterial wall in relation to blood lipids, hormonal and physical factors.

Factors affecting intra-vascular thrombosis and thrombolysis.

3.4.3 *Treatment*

Controlled population studies on the effects of diet on the development of atherosclerosis in relation to blood lipid levels.

Long-term effects of treatment of hypertension on complications due to atherosclerosis.

Further studies of the preventive and therapeutic value of anticoagulants.

A study of rehabilitation in the acute stage of myocardial infarction, including the effects of early ambulation.

4. SUMMARY AND CONCLUSIONS

(1) An attempt has been made to clarify those aspects of arterial hypertension and ischaemic heart disease which might provide a working basis for preventive measures in these conditions.

(2) Methods of blood pressure determination are discussed, with special reference to "casual" and "basal" pressures. The Committee reiterates the recommendations of the Expert Committee on Cardiovascular Diseases and Hypertension¹—namely, that in the auscultatory method the inflatable bag should be 14 cm wide, and long enough to encircle the arm.

It considers that both the point of muffling and the point of disappearance of sounds should be recorded as the diastolic pressure until investigations clarify this problem.

(3) Classification of arterial hypertension into three stages is proposed, with a view to separating individuals who need regular supervision and treatment; methods of differential diagnosis of essential and renal hypertension are described. It is hoped that improved classification and diag-

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1959, 168.

nosis will make it possible to standardize screening procedures, and will yield more comparable data from studies in different parts of the world.

(4) A classification of ischaemic heart disease is put forward, suitable for trials in prevention and control. The diagnostic features of the various clinical groups are summarized for purposes of screening, and the factors which may lead to a predisposition to the disease are discussed.

(5) There are as yet no effective means of preventing the occurrence of either arterial hypertension or ischaemic heart disease. Furthermore, the therapeutic remedies at our disposal are not simple, and may seriously affect the personal and social activities of the subject. At the present time, therefore, large-scale preventive measures are difficult and may be unwise until their value is more clearly known. Nevertheless, in the individual patient, progression of the disease and complications can often be delayed or prevented by appropriate treatment.

(6) Subjects for research in various fields are suggested. In both diseases, progress in prevention will remain limited in scope until more information is available on the problems of etiology, early diagnosis and natural history. Relatively small-scale studies in different areas are recommended for this purpose, and also to test preventive measures. Such studies may serve as models for more extensive application.

(7) There is in all fields a great need for international co-operation, and the Committee noted with satisfaction that the present WHO programme in arterial hypertension and ischaemic heart disease is orientated to a large extent towards promoting and co-ordinating research. The general lines along which WHO might facilitate further investigation have been indicated in the report.

Continuing efforts should be directed particularly towards improvements in methodology, in order to establish standardized or comparable procedures and techniques in different countries. Examples are: the early diagnosis of ischaemic heart disease, methods of blood-pressure recording, differential diagnosis of arterial hypertension, methodology in investigating the effects of environmental stress, and more accurate death certification.

Some specific problems pertinent to research in arterial hypertension and ischaemic heart disease can be dealt with effectively by small groups of experts drawn from different disciplines, and WHO can play a most valuable role in convening these meetings.

Finally WHO will contribute considerably by promoting in national programmes the implementation of measures outlined in this report.

Annex 1**METHODOLOGY OF RENAL INVESTIGATION
IN ARTERIAL HYPERTENSION**

It is not intended to overemphasize the part played by renal disease in the general problem of hypertension, but the details which follow are included to provide information on methodology in a subject which is not generally well understood.

When proteinuria is found in a hypertensive subject, the examination should be repeated on a timed overnight specimen. This serves to exclude postural proteinuria, and the concentration of protein gives a preliminary indication of the differential diagnosis. Protein excretion exceeding 1 g per 24 hours is more likely to be due to primary renal disease than to essential hypertension (except in the malignant phase). A past history of acute nephritis or the nephrotic syndrome corroborates the diagnosis. With smaller degrees of proteinuria, further investigation is necessary.

The following investigations are desirable :

- (1) Twenty-four-hourly protein excretion (requirements : measuring cylinder, Esbach tube).
- (2) Qualitative examination of a freshly collected, hand-centrifuged specimen for erythrocytes, leucocytes and granular casts. If possible, quantitative examination of these (Addis count). Requirements : centrifuge, a graded centrifuge tube, a blood-counting chamber, a microscope.
- (3) Bacteriology of urine, if possible quantitative, on a clean non-catheter specimen.
- (4) Three-hour creatinine clearance as screening test. Twenty-four-hour clearance if this is abnormal. Requirements : colorimeter.
- (5) Urine concentration test (specific gravity of urine collected at four-hour intervals over a period of 30 hours' fluid starvation). A minimum specific gravity of 1028 is obtained during this period in at least one specimen in almost all subjects with normal kidneys. Requirements : densitometer.

Under special circumstances, these data may be supplemented by the following investigations :

- (6) Intravenous pyelography, cystoscopy and retrograde pyelography.

¹ It is undesirable to use a catheter to obtain specimens of urine for diagnostic purposes. In women, satisfactory clean specimens can be obtained by the tube technique described by Leather, H. M. & Hutchings, M. I. (1960) *Lancet*, 2, 654.

- (7) Creatinine concentration in the urine collected from each kidney, or if possible the performance of separate renal clearances.
- (8) Aortography.
- (9) Renal biopsy.

Annex 2

THE DIFFERENTIAL DIAGNOSIS OF ESSENTIAL AND RENAL HYPERTENSION

In *essential hypertension* (excluding the malignant phase), proteinuria is usually less than 1 g per 24 hours, the urinary deposit contains very few erythrocytes and leucocytes, and practically no casts (less than 100 000 per 24 hours). Concentrating power is either normal or is not reduced proportionately with glomerular filtration. The urine is sterile, the intravenous pyelogram reveals no abnormalities, the creatinine concentrations in the urine from the two kidneys differ by less than 12%. In the late stages haematuria may occasionally occur and atherosclerotic changes may lead to reduced glomerular filtration rate and even some degree of nitrogen retention.

In *chronic pyelonephritis* the urine usually contains less than 1-2 g of protein per 24 hours; leucocytes are increased in number and predominate over the other elements in the urinary deposit in most cases. Casts do not exceed 1×10^6 per 24 hours. Concentrating power is reduced disproportionately as compared with glomerular filtration rate. Urinary bacterial cultures are positive in over 80% of cases, and the infection is massive (100 000 or more per 1 ml urine). Pyelography reveals important abnormalities in the majority of instances. Creatinine concentration in the urine from the two kidneys differs almost always by more than 12%.

A similar functional pattern may also be produced by *polycystic kidneys*, but the clinical features and X-ray findings in such cases are diagnostic.

Chronic glomerulonephritis is usually accompanied by a more severe degree of proteinuria, a urinary deposit containing erythrocytes predominantly, but with a marked increase also in leucocytes and casts. Concentrating power is usually reduced proportionately to glomerular filtration; the urine is sterile. Creatinine concentration in the urine from the two kidneys does not differ, and radiologically cortico-medullary differentiation is obscured. In long-standing cases proteinuria may be slight and inflammatory elements are absent from the urinary deposit until the terminal stages, when severe secondary hypertensive damage occurs.

In hypertension due to a *stenosed renal artery* the urine may be free from protein, but the diagnosis should be suspected in cases of severe or malignant hypertension in young adults, in the absence of a family history of hypertension, and in long-standing cases if the hypertension suddenly becomes more severe or changes to the malignant course. In the absence of pyelonephritis, a difference in size of the two kidneys, detected on X-ray examination, also suggests the diagnosis. A bruit, which is best heard in the epigastrium or lateral to the umbilicus, is a valuable clinical sign. Renal angiography (aortography) is necessary to establish the diagnosis.
