sputum was greenish yellow, and both pneumococci and tubercle bacilli were found. Meanwhile the pathological report on the fluid aspirated from the chest also indicated that pneumococci were present in the effusion, further investigation revealing that it was a Type II infection. Blood culture was negative.

Despite the usual routine treatment, supplemented by oxygen administration and cardiac stimulants, the patient's condition rapidly deteriorated, and by July 9 he was almost comatose. He was very cyanosed and toxic, and the sedimentation rate showed a further drop to 32. At this stage a supply of M & B 693 tablets was obtained, and a dosage of two tablets (1 gramme) given every four hours, with a total of 5 grammes daily. The next day his temperature had dropped from 101.2° to 99° F., and the pulse rate improved both in rate and force. Subsequently the temperature continued to show a steady fall (see chart), and the improvement in his condition was dramatic. After five days, the patient's temperature having now been normal for more than forty-eight hours and a total of 25 grammes of the preparation having been given, the drug was discontinued. But on the third day after the cessation of the tablets both temperature and pulse rate began to rise once more, and the patient was not so well. One gramme was therefore given at four-hourly intervals once more; but after three days the tablets were again discontinued, as the pulse and temperature were back to normal and the occurrence of toxic effects of the drug was feared. From this point he made a steady recovery and remained afebrile for another month, at the end of which time his sedimentation rate had improved to 15, and radiography of the chest revealed that except for thickened pleura over the lower half of the right lung, with obliteration of the costo-phrenic angle on this side, there appeared to have been no ill effects upon the lung tissue as a result of the pneumococcal infection and the subsequent effusion. The tuberculous lesion itself appeared to be much more fibrotic, and there was an absence of the fluffy, mottled shadows which had been noted on admission.

It should be added that pneumococci were still present in the sputum the day that treatment was begun with M & B 693, but that they could not be found on the third day and remained absent at each subsequent examination. The leucocyte count dropped from 12,000 to 7,600 per c.mm. on the fifth day of treatment with the tablets, but an increase in the red-cell count from 4,200,000 to 5,800,000 per c.mm. was noted.

Pulse and temperature chart showing effect of administration of M & B 693. The thick black lines indicate the period during which the preparation was given. The arrow indicates the aspiration of the chest which was performed. The figures within the circles indicate the blood sedimentation readings (Cutler technique).

Commentary

The development of pneumococcal pneumonia in the course of pulmonary tuberculosis is a comparatively rare occurrence and must be considered an ill omen. Although cases have been noted in which recovery from a genuine lobar pneumonia superimposed upon a tuberculous lesion has occurred, in the case described above the condition of the patient was so bad that it was not expected that he would live for many hours after the sixth day of his illness.

No benefit was being obtained from routine treatment until M & B 693 was given, when a dramatic recovery followed.

The initial dosage was not high because we did not know what effect the presence of a tuberculous process in the lungs would have on the patient's response to the preparation, but no toxic effects at all were observed during the administration of the tablets, and in all probability higher doses could have been given with safety. The discontinuance of the drug after five days was apparently a little premature in this case, but the slight relapse which followed was easily controlled by further administrations of the tablets in the same dosage as before.

A further interesting point is that no increase in activity of the tuberculous disease occurred as a result of the infection, and that subsequent radiographic investigation of the chest revealed a definite improvement in the nature and extent of the lesion. The actual course of the pneumonic infection, and the patient's response to treatment, were clearly shown by the different blood sedimentation results during the course of the disease.

I have to express my thanks to Dr. J. B. McDougall for much helpful advice and for permission to publish this case, and to Messrs. May and Baker for a supply of the tablets M & B 693.

THE PROGNOSTIC SIGNIFICANCE OF OPHTHALMOSCOPIC FINDINGS IN CASES OF HIGH SYSTOLIC BLOOD PRESSURE

A REVIEW OF 83 CASES

BY

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High blood pressure is a common finding in the course of the routine examination of patients. It is usually regarded as a serious sign, and I think rightly so. But all cases are not equally serious, for numbers survive for years in a good state of health. It was to learn something about the outcome in such cases that the present investigation was undertaken, and particularly to discover whether or not the ophthalmoscopic examination might help in the differentiation of cases from a prognostic point of view. Eighty-three unselected cases have been followed up, the only standard for their inclusion in the series being a systolic blood pressure of 170 mm. Hg or over, as measured by the auscultatory method over the brachial artery. To have chosen the systolic pressure only is not to imply disregard of the importance of the diastolic pressure. This of itself is probably of more importance than the systolic pressure. But the diastolic pressure cannot be ascertained in a certain proportion of cases (Beaumont and Dodds, 1931), and it is not certain that all observers would agree as to its exact level in any given case. The systolic pressure is that upon which most clinicians base a diagnosis of high blood pressure. For these reasons, therefore, and because in an investigation of this kind it is easier to refer cases to one criterion than to two, it was decided to make systolic pressure the standard. The cases have been under observation for periods of up to five years, the average being two and a half years. Two points were chosen for special observation: (1) the state of the retinal blood vessels and (2) the presence of deposits—namely, exudates and haemorrhages.

State of the Retinal Blood Vessels

The classical signs of arterial degeneration were present in varying degrees of severity in many of the cases—namely, burnished copper-wire appearance, tortuosity and irregular calibre of the arteries, and deflection and constriction of the veins at the arteriovenous crossings. Most observers agree that these signs are commonly found in such cases. In addition, however, two features were noticed which are not generally remarked upon: (1) A haze overlying the arteries at points, especially at the arteriovenous crossings, and obscuring the vessel wholly or partly: I have not seen this commented upon elsewhere. (2) Attenuation of the blood stream in the arteries to the point of complete obliteration in some cases and of reduction to a mere thread in others. This latter feature has, however, been recorded by a number of observers, but it does not seem to have received universal recognition. A decrease in the lumen of the arteries appears to be one of the essential changes in these cases, and, in my opinion, its degree is a valuable index of the stage to which arterial degeneration has progressed. An attempt has been made to grade the appearance of the retinal blood vessels according to the degree of abnormality present, thus:

First degree.—Copper-wire appearance of arteries only, or normal appearance.

Second degree.—Tortuosity of arteries. Deflection and constriction of veins at arteriovenous crossings.

Third degree.—Irregular and reduced calibre of arteries.

Fourth degree.—Haze overlying the arteries at points, and especially at arteriovenous crossings.

Fifth degree.—Marked attenuation of blood stream, causing thread-like appearance in one or more arteries.

As a general rule the characteristics of any particular degree are in addition to the characteristics of the preceding degrees, but this is not invariably so. Thus the fifth degree does not always include haziness, belonging to the fourth degree, or copper-wire appearance, belonging to the first degree. It was a matter of some doubt whether the fourth or the fifth degree was really the more severe, but I considered that the thread-like attenuation of the arteries presented in appearance the greater departure from normality.

The following table shows the incidence of death and of cerebral haemorrhage in each degree group, and also the average systolic blood pressure relative to each group.

Group	No. in Group	Deaths	Cerebral Haemorrhage	Average Systolic Blood Pressure
First degree	18	—	—	mm. 190
Second „	26	—	—	205
Third „	22	—	2	209
Fourth „	9	1	4	221
Fifth „	8	2	7	229

A study of this table reveals a close relation between the degree of retinal arteriosclerosis and the incidence of deaths and of cerebral haemorrhage. Of those cases exhibiting fifth degree sclerosis seven-eighths developed signs of cerebral haemorrhage within the period of observation, with an average of two and a half years. The table also shows the relation which exists between the degree of sclerosis and the height of systolic blood pressure. Figures relating to the latter are, however, only averages, and the correspondence does not necessarily

apply to each individual. The incidence of cerebral haemorrhage was worked out for individuals in the series having a systolic blood pressure of over 220 mm., and it was found to be nine out of twenty-eight—approximately one-third. These figures would appear to indicate that the degree of vascular degeneration as observed in the retinal blood vessels affords a much more accurate index of the gravity of a case than the systolic blood pressure of itself, and suggests that in cases of high systolic blood pressure those showing retinal arteriosclerosis of the fifth degree are the most liable to cerebral haemorrhage, and that they are likely to have a “stroke” within a period of about two and a half years.

Other observers, notably Brana and Radnai (1935), have made investigations similar to the above and with the same object in view. They describe three degrees of retinal arteriosclerosis, the first degree showing variations in the calibre of the arteries, the second showing more numerous variations with distinct narrowing of the arteries, and the third showing striking narrowing. They note a certain degree of correspondence between the systolic pressure and the gravity of the fundus changes. As regards prognosis their findings are based upon the observation of 100 cases, followed up over the course of one year, and these are: with normal fundus, life is not endangered; with second degree sclerosis, 60 per cent. of deaths; with third degree sclerosis, 100 per cent. of deaths. While these figures indicate a much greater mortality than that found in the present series, they bear out the same conclusion—namely, that the retinal blood-vessel changes afford a most valuable index to prognosis in cases of high blood pressure.

Bonnet and Bonamour (1936) state that “it is possible to tell the stage of evolution of the clinical condition of the patient”—that is, from the condition of the retinal vessels. The prognosis, they say, may be assessed from this, and they quote Dumas in support of the view that the prognosis does not depend upon the height of the blood pressure. Conclusions are based upon a study of 100 cases, but no figures are given. Foster Moore (1925) records fifty-two cases attended at Moorfields for symptoms dependent upon retinal arteriosclerosis, their condition being ascertained after seven years. Seventeen of these patients died of cerebral haemorrhage or thrombosis, and, in addition, six developed vascular lesions of the brain—that is, twenty-three out of fifty-two, or 44 per cent., had vascular lesions of the brain within seven years. In the present series, in the group representing the three most severe degrees of retinal arterial degeneration and comprising thirty-nine cases, thirteen (33.3 per cent.) had vascular lesions of the brain within the period of observation, the average of which is two and a half years.

Presence of Deposits in the Retina

EXUDATES

Twenty-two cases (26.5 per cent.) exhibited this feature. In twenty-one of these the exudates were of the nature of small white dots, discrete in all except one case, in which they were confluent. Characteristically these were circular in shape, and surrounded by a faint dark halo. They were aggregated in the macular area in all except two cases, in one of which they were scattered and in the other arranged round the central area of the fundus. In no instance was there a stellate or fan-shaped arrangement round the macula. In some cases the dots were thought to bear a topographical relationship to the terminal twigs of the retinal blood vessels. These

observations accord closely with the description given by Bonnet and Bonamour (1936), who mention the shaded edges, and also the relation to the terminal macular vessels. There is no doubt that these spots correspond also to the type described by Foster Moore (1925) as belonging to the picture of arteriosclerotic retinitis.

Three of the cases showing exudates—that is, one-seventh—developed signs of cerebral haemorrhage; so that the presence of exudates would not appear to be of such serious prognostic significance as high systolic blood pressure by itself (one-third of the cases over 220 mm.), nor is it comparable to retinal arterial degeneration (seven-eighths of the fifth degree group). The urine was examined in nineteen cases having exudates. Albumin was present in three cases only. There was a reduction of Fehling's in one case. Of the remaining cases not showing retinitis forty-four had the urine examined, and albumin was present in eight. There was a reduction of Fehling's in two cases. This type of retinitis would appear, therefore, to be independent of the presence or absence of albuminuria or glycosuria.

It is interesting to note that none of the cases showed the type of retinitis usually associated with renal disease—namely, star figure at the macula, cotton-wool patches, etc.—or the type usually associated with diabetes mellitus; for it is argued by some that these types of retinitis are an outcome of the high blood pressure only and not of the associated disease. Here we have a series of eighty-three cases of high blood pressure not one of which showed the classical signs of renal or diabetic retinitis. This does not, of course, argue that high blood pressure has no influence in the production of these types of retinitis; but it does argue that it is not the sole cause. It may be said of the type of retinal exudate under consideration that it points to the probable existence of high blood pressure but that of itself it has little prognostic significance.

RETINAL HAEMORRHAGES

These were noted in six cases. They seem to bear little relation to the height of the systolic blood pressure and do not of themselves appear to be of serious import. None of the six patients exhibiting the sign died or was the subject of cerebral haemorrhage.

Conclusion

The chief conclusion to be drawn from this study is that in cases of high systolic blood pressure the retinal arteries provide a reliable index of the state of the cerebral arteries and furnish an accurate means of foretelling which cases are most liable to vascular accidents of the brain. It confirms the time-honoured adage that a man is as old as his arteries, and suggests that the best means of ascertaining the age of his arteries is to inspect those accessible to direct vision in the fundus oculi.

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At the French Colonial Office an advisory committee on trypanosomiasis has recently been appointed with the task of studying this disease from every aspect and proposing any remedy which may be useful. Its fourteen members are appointed by the Colonial Minister.

A CLINICO-PATHOLOGICAL CLASSIFICATION OF CANCER OF THE BREAST

BY

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Reference to the literature concerning the late results in the treatment of carcinoma of the breast has revealed an urgent need for the adoption of a uniform system of classification of patients according to the stage of the disease at the time of treatment. When a careful study is made of the statistics from various clinics it is obvious that different methods have been used in the classification of cases. It is true that in many papers no attempt has been made to classify according to the extent of the disease, and early and advanced cases have been considered together. While such figures are of interest as showing the fate of a large number of patients, no indication is given of the value of the several methods of treatment adopted. With the continued evolution of treatment in carcinoma of the breast and the development of irradiation methods, either alone or in conjunction with excisional procedures, it has become necessary to compare the end-results accruing from each method in order that still further advance may be made. For the appraisal of these techniques it is essential that comparable groups of cases according to the extent of the disease should be considered. The value of such a classification in carcinoma of the breast is exemplified by what has been achieved in carcinoma of the cervix uteri. When irradiation began to be used in the treatment of that disease it became apparent that the end-results must be compared with those obtained by excisional methods. As a result a classification was evolved whereby the results of each method of treatment could be compared in the same stage of the disease. With further knowledge concerning the life history of carcinoma of the cervix uteri certain modifications in the classification have been made, and now in many countries in Europe a uniform method is used, so that it is a safe and easy matter to compare not only the results obtained from various clinics in one country but the results obtained in each country.

The Need for Uniform Classification

Up to the present no uniform classification has been adopted for cases of carcinoma of the breast. If such a plan were adopted by clinics much useful information would come to light concerning prognosis in this disease and the relative values of the various therapeutic measures carried out. Further, there would be greater uniformity in the publications relating to treatment. As a result of work carried out in the follow-up departments of St. Bartholomew's Hospital and of the Royal Cancer Hospital (Free), I have evolved a classification based upon a correlation of the interrelated clinical and pathological aspects of cancer of the breast. Many attempts have been made to evolve a satisfactory system of classification both on clinical and on pathological grounds. Steintal (1905) published a method which has received wide attention. This classification is as follows. Stage I: Slowly growing tumour, only a few centimetres in diameter, confined to the breast; no attachment to skin; the axillary nodes are few in number and are first discovered at operation. Stage II: A tumour which, after remaining stationary for some time, begins to increase in size; there is attach-