EARLIEST SYMPTOMS OF DISEASES OF THE MACULA*†

BY

MARC AMSLER

Zürich

FROM whichever side it is approached, the question of diseases of the macula presents great interest and merits attention, because macular diseases are both common and serious.

Diseases of the macula are common. In the first place I am thinking of senile maculopathy in its various forms. It is beyond doubt that the demographic trend of progressive ageing of the population is producing a very real increase in the number of cases of senile macular degeneration: to such a degree that we find ourselves—as ophthalmologists—involved in the science of “gerontology” and “geriatrics”.

I am thinking, too, of myopia of medium and high degrees, the complications of which frequently compromise central vision long before advanced age is reached.

Even though exudative maculopathies in adults are less widespread, and juvenile and familial macular degeneration is relatively rare, this is not the case in those lesions of the macula which occur in the course of retinopathies associated with hypertension, diabetes, periphlebitis, venous thrombosis, and so on, or again as a complication of chronic iridocyclitis.

Diseases of the macula are serious. In injuring one of man's most precious functions, maculopathies attack him in one of his very sensitive spots, making him not only an invalid, but a particularly unfortunate one. It is certainly not an exaggeration to say that a central scotoma can destroy a professional career and disturb the normal activity of any life.

And what can our therapeutic agents avail against one or other of these progressive lesions of the central retina? The seriousness of a maculopathy is a direct measure of our impotence to restore vitality to tissues already destroyed, especially to the delicate, highly differentiated sensory or pigmented epithelium.

METHODS OF INVESTIGATION

Since the invention of Helmholtz (whose centenary we have just celebrated), four or five generations of ophthalmologists have concerned themselves with observing, describing, drawing, and photographing a multitude of morbid conditions of the macula. We have differentiated various ophthalmoscopic pictures, out of which have emerged a corresponding number of morbid

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states. To distinguish them we have given them names, some of which call up a particular morphological aspect (circinate retinopathy, disciform degeneration, pseudo-tumour of the macula, honeycomb-macula), while others have a pathological significance (central angiospastic retinopathy, central serous choroido-retinopathy, macular capillarosis). Associated with these is a galaxy of famous names, including those of Förster, Hutchinson, Fuchs, Mackay, Nuel, Doyne, Haab, Vogt, Coppez and Danis, Junius and Kuhnt, Horniker, Kitahara, Bailliart, and Duggan.

Glancing at the development and perfection of the methods of investigation of the fundus in general and of the macula in particular, we see, by the second decade of the 20th century, three methods of examination, each complementary to the other, which combine to enrich our knowledge of the morphology of macular lesions.

(i) Gullstrand (1911) produced the first binocular and stereoscopic ophthalmoscope which introduced the third dimension into our examination of the macula.

(ii) Vogt (1913, 1918) used red-free light the value and usefulness of which even to-day we cannot overestimate: the macula displays its yellow colour more or less intact, and we are able to localize it in the midst of the various lesions which occur at the posterior pole of the eye, the opaque retina concealing any coincident choroidal changes, but, on the other hand, demonstrating clearly the pattern of its fibres and the finest ramifications of its vessels.

(iii) Koepe (1918) gave us the focal illumination of the slit lamp for fundus examination, a technique recently perfected by Goldmann and by Hruby, which enables us to observe the smallest change of level, particularly in the macular region.

What then is the purpose of this achievement of technical perfection if not to allow us to follow, in all their delicacy and intimacy, the changes in the nervous tissues and the vessels at the macula in pathological conditions, and to anticipate, as far as possible, their progress? But here questions of fundamental importance arise.

Does the initial ophthalmoscopic picture of a disease of the macula correspond to the initial visual disturbance which brings the patient to consult us? Do we always find with the ophthalmoscope an organic change at the macula which explains the functional disturbance in question? We all know by experience that this is not the case. An ophthalmologist, no longer amongst us, who was known as a master of accurate ophthalmoscopic observation, one day snubbed a patient who began to describe a recent and subtle visual disturbance: "Please be quiet", he said, "I will soon see what your trouble is".—"There is nothing the matter" was the verdict after a long and careful examination. But that patient definitely had a disturbance in the form of a slight instability of central vision, a purely functional symptom, which preceded the occurrence, a few months later, of an organic maculopathy, a serious development which I was able to follow myself.

IMPORTANCE OF THE PATIENTS' OWN OBSERVATIONS

The literature shows that although modern work, founded on the ophthalmoscopic appearances and histopathology of established maculopathies, pays little attention to the functional disturbances which accompany these diseases, older authors, less privileged than ourselves from the technical point of view and undoubtedly less pressed for time, gave much more attention to the explanations and complaints of their patients: they helped them to analyse their visual disturbances, made them draw them, and endeavoured to reconstruct and interpret their subjective symptoms. See, for example, the publications of Förster (1862), Knapp (1869), and Wundt (1898). These old authors interested themselves especially in metamorphopsia as one of the earliest and most characteristic signs of myopic and senile maculopathies. They ask us to do as much.

At Oxford in 1949, I described the case of a patient who replied, after I had told him that he had 6/6 central vision in spite of his complaints: "Yes, I see your small letters, but their quality is missing" (Amsler, 1949).

From this we see that there are *qualitative* disturbances of vision which escape our ordinary quantitative methods of examining central visual acuity. These quantitative examinations, though practical, are on the whole rather crude, for through their apparent precision a visual acuity of 3/6, for example, is compatible with qualitative disturbances of great variety. But it is precisely visual disturbances of this kind, subtle and often transient, which precede ophthalmoscopic changes. Medical science to-day recognizes that in every field functional disturbance precedes the evident organic lesion, and appreciates also that a functional disturbance has more chance of being reversible than an established organic lesion. The old adage *principiis obsta* is of particular value to us, because the sensory organ with which we are concerned lends itself to a self-observation particularly sensitive to the slightest functional failure, and this early failure makes the *principia* on which we should open our therapeutic counter-offensive.

Let us record another fact of everyday experience. This functional disturbance and its variations, provided sufficient attention is paid to it, is a far more sensitive guide to the course of any maculopathy than changes in the ophthalmological picture of the lesion. How often do our patients describe an increase or decrease in visual acuity without our being able to find any ophthalmoscopic sign to account for these changes!

THE EARLY SYMPTOMS OF DISEASE

What then are the first symptoms of diseases of the macula and how can we record them? These early functional symptoms consist on the one hand of *metamorphopsia* (which I shall call *metamorphoma*) and on the other of a *relative scotoma* (which I prefer to call a *translucid scotoma*).

For the purpose of recording these subtle disturbances, our visual charts, with their quantitative scale for distance and reading, are inadequate. How can we reveal the metamorphoma of a high myope who can no longer read

easily, or the scotoma of a patient who persists in rubbing his eye to improve his vision, telling us at the same time this revealing fact: "I should be able to see the letters easily if it were not for the fog in front of my eye". We should seek methods of following up these clues provided by our patients.

Let us note that these two early symptoms of maculopathy, metamorphoma and relative scotoma, either fail to be revealed by the perimeter and the Bjerrum screen or are recorded inaccurately. Even if we manage to plot a relative scotoma by means of patient exploration with very small targets and low illumination, metamorphoma always eludes a campimetric or perimetric examination. Since it is a matter of making apparent some kind of deformation, we must present to the patient a precise and regular contour which forms as simple a figure as possible, the alterations of which he can assess without difficulty.

FIG. 1.—The Amsler Grid.

A SIMPLE METHOD OF EXAMINATION

The essential points of a practical and rapid method of examination are these (Amsler, 1947, 1949):

FIG. 2. — The grid within the visual field.

The eye under examination is presented at reading distance (28–30 cm.) with a black card, or better still a school-slate (Fig. 1). On this is drawn in white a 10-cm. square subdivided every 5 mm. by vertical and horizontal parallel lines, thus giving the appearance of a perfectly regular grid. Each small 5-mm. square subtends an angle of 1° at 28–30 cm. distance. The entire grid is thus 20° high and 20° wide, 10° each side of the centre. When it is introduced into the visual field (Fig. 2), its image occupies only a small central area of 10° surrounding the point of fixation, but this area is the most important of the whole. The blind spot lies outside the grid.

When the image of the grid is projected on to the fundus, always at a distance of 28–30 cm. (Fig. 3), it occupies

FIG. 3.—Image of grid projected on to the fundus.

FIG. 4.—Dimensions and extent of optic disc and macula in relation to the image of the grid.

a greater area than the macula and fovea, the optic disc is found about 5° outside its nasal limits, and only the finest vascular branches (too fine to give rise to the smallest angio-scotoma) penetrate into its projection.

Finally, it is not without interest to consider the dimensions and extent of the optic disc and macula in relation to the image of the grid (Fig. 4). We see here in the middle of the oval fovea, two small concentric circles: the inner one, 200μ in diameter, marks the foveola, the outer, 400μ in diameter, outlines the avascular area of the macula, such as one can see entoptically by means of the Scheerer-Zeiss apparatus, which shows so clearly the capillary circulation in the cerebral layers of the retina.

Returning to the grid* we present it, under a good illumination, to the eye in which we wish to analyse the visual disturbance after the refractive error is carefully corrected. Then we proceed to ask the patient questions: first those which relate to metamorphoma, and then those which are aimed at bringing out the perception of a relative scotoma.

(1) *Metamorphoma*.—"Are the lines which cross in the grid straight and absolutely parallel from beginning to end, especially near the centre?"

"Are all the small squares regular and perfectly equal?"

The patient must, of course, fix the central point of the grid and not let his eye wander, and he must understand what is meant by excentric vision. He will be helped in this by repeated comparison with the other eye. This eye may be healthy and normal and if diseased it will almost certainly not have exactly the same changes in central or paracentral vision as its fellow.

The first thing which strikes us in the course of these examinations is that metamorphoma rarely occupies the entire grid; it almost always occurs in one or sometimes many distinct regions, so that the patient has no difficulty in localizing and determining these foci of metamorphoma which I call, in analogy with scotomata, metamorphomata. The nearer the *metamorphoma* is to the fixation point (it is often central and surrounds it) the easier it is for the patient to observe and describe its character (Figs 5 and 6). There are various forms of metamorphoma; sometimes the lines are broken into small angular irregularities, sometimes they are curved into smaller or greater undulations. The first visual disturbance

FIG. 5.—The first metamorphoma illustrated in the literature (Förster, 1862).

FIG. 6.—Metamorphoma close to the fixation-point; its localization at the right side makes the reading difficult.

* Which forms a part of a series of seven charts published by Hamblin.

which announces a maculopathy can consist of only one small juxta-central deviation of either the vertical or the horizontal line. If this deviation is found astride the fixation point itself or to its immediate right, it is easy to understand the difficulty in reading.

Sometimes the patient indicates that instead of a definite deformation there is an instability of vision, as if the network of the chart were seen through a sheet of moving water. This also is a manifestation of finest metamorphoma, and is brought about by slight unconscious and involuntary movements of the eye in an effort to see the picture with which it is presented.

A particularly curious phenomenon, already observed and described by Förster (1862) and Mackay (1894), is the orientated metamorphoma. In central or paracentral metamorphoma either the horizontal or the vertical lines only show undulations. To detect this type of metamorphoma, another of my charts presents parallel lines in one direction only, and the patient fixes them successively in the horizontal, the vertical, and the various oblique positions (Fig. 7).

Micropsia, which is fairly frequent, and macropsia, which is rarer, are special types of metamorphoma. Here the metamorphoma is orientated round a centre which is almost always the fixation point. In micropsia (Fig. 8), the vertical and horizontal lines curve inwards toward the central point, in macropsia away from

First Experiment:—Hold thus—lines vertical.
FIG. 7.—The first test-lines illustrated in the literature (Mackay, 1894).

FIG. 8.—Microptic central metamorphoma (macular oedema).

it. The foci of micropsia or macropsia can be very small, occupying only one or two small squares, or they may be much larger, occupying ten lines or more. In place of the ordinary metamorphomata which the patient localizes within the grid, it sometimes happens that he describes a generalized metamorphoma, more or less orientated, which deforms the entire grid to such an extent that its margins are no longer parallel and its internal lines bent into large, more or less regular, waves. This may be called diffuse metamorphoma.

These different types of metamorphoma correspond more or less to different types of maculopathy.

The small angular defects in the lines of the grid are characteristic of myopic maculopathy; the beginning of senile maculopathy is generally shown by undulations. Diffuse metamorphoma is encountered in detachment of the retina, which starts, for example, as a disinsertion at the ora serrata and spreads to the macular region. When the macula has been detached, and even long after its re-attachment by operation, the patient describes an irregularity of the grid in which the lines look as if they had been drawn free-hand—by an unsteady hand. (Fig. 9).

(2) *Relative, or Translucid, Scotoma*.—"Do you see the grid anywhere perfectly clear and without spots?"

"Is the region round the central point as clear as the periphery of the grid?"

(In case there is a spot) "Are the lines in the spot completely absent or only veiled and perhaps interrupted?"

The net which is thrown, like a butterfly-net, before the patient's eye to catch any visual disturbances sometimes catches a spot which is usually central and circular (or slightly oval or pear-shaped) and which usually measures about 10–12

FIG. 9.—Diffuse metamorphoma after a successful detachment operation.

FIG. 10.—Central translucid scotoma, of usual shape and size.

small squares across. This spot is translucid; it does not completely hide the crossing lines of the grid but covers them with a veil which is sometimes homogeneous and sometimes more opaque in one place than in another. It is the presence of this translucid central scotoma which gives rise to the patient's habit of rubbing his eye in a vain effort to improve his vision (Fig. 10).

This translucid scotoma can also be excentric, when it is smaller and often multiple; the patient indicates these spots, which are irregularly placed, with his finger. The farther these spots are from the centre, the greater his difficulty in determining their shape.

If often happens, in either the first or subsequent examinations, that the patient shows a combination of metamorphoma and translucid scotoma. This combination may be made up of many variations. Sometimes the metamorphoma, especially the microptic type, coincides with the scotoma so that lines are only

distorted within the translucid scotoma; sometimes the metamorphoma is appreciated in a more or less circular zone surrounding the scotoma; sometimes metamorphomata occur quite independently of the central translucid scotoma.

UNDERLYING PATHOLOGY

Let us now turn to the significance of these metamorphomata and translucid scotomata and ask ourselves what is the *structural basis* underlying them. Histopathology will never help to solve this problem. Even if we had the opportunity to examine a macula microscopically at this stage, death, chemical fixation of the globe, and the manipulations of the laboratory would certainly have destroyed or fundamentally modified the delicate microstructure of the macular retina and its sensory elements. Nor can the early stages of these symptoms be established by an examination of sections of established macular lesions.

In point of fact, it is at the level of the pigmentary epithelium and the sensory epithelium of the macular retina, which together make up the anatomico-physiological couple of visual perception, that we must look for the organic basis of metamorphomata. They result, I believe, from a displacement of the perceptual elements of the retina and a false localization of the image seen by these displaced elements. This pathogenic explanation of metamorphoma is generally attributed to Förster, but Mackay (1894) pointed out that the merit belongs to Reid who explained in this way his own metamorphoma which caused a considerable disturbance after he was dazzled by the sun in the course of an astronomical observation in 1761. Here are Reid's own words:

... A straight line appears to the right eye to have a curvature in it. Thus, when I look upon a music book, and, shutting my left eye, direct the right eye to a point of the middle line of the five which compose the staff of music, the middle line appears dim indeed at the point to which the eye is directed, but straight; at the same time, the two lines above it and the two below it appear to be bent outwards, and to be more distant from each other and from the middle line, than at other parts of the staff to which the eye is not directed (Reid, 1801).

Reid advanced the following hypothesis to explain the curving of the lines of the staff of music:

To me it seems probable that a small part of the retina towards the centre is shrunk, and that thereby the contiguous parts are drawn nearer to the centre and to one another than they were before, and that objects whose images fall on these parts, appear at that distance from each other which corresponds not to the interval of the parts in their present preternatural contraction, but to their interval in their natural and sound state.

It was not until one hundred years later that Förster reached a similar conclusion: when two parallel lines are separated from each other by an outward curve it means that the retinal elements are approximated to each other at this point. Macropsia is thus the outcome of retinal contraction.

Micropsia, always present in central serous chorio-retinitis (Oguchi, 1922; Kitahara, 1936; Horniker, 1927; Bonnet, Paufigue, and Bonamour,

1939; Streiff, 1939; and above all Brückner and Field, 1945), is the opposite case. The oedema raises and distends the basal attachment of the cones and separates them so that fewer perceptive elements are stimulated; thus the object appears smaller than it really is, and micropsia results.

What is it which displaces and separates the elements of the sensory epithelium of the macular retina? There is no doubt whatever that it is a fluid agent. These metamorphomata of changing dimensions and shape, which disappear and re-appear, can only be due to the action of a liquid. On the other hand, we know that amongst the most constant changes, histopathology of advanced macular lesions shows spaces, lacunae, cysts, and other formations, where during life fluid collects or possibly circulates.

What is this fluid and where does it come from? In the first place, we must postulate an oedema produced from the chorio-capillaris, the outcome of a transudation or exudation through the changed walls of the capillary network which nourishes directly the pigmentary and the visual epithelium. The chorio-capillaris is modified by the senile changes of sclerosis and its walls become permeable. The fluid which transudes into the sensory retina displaces the perceptual elements and gives rise to metamorphomata.

We can visualize, in an analogy with our knowledge of oedema elsewhere in the body, that the fluid which displaces the macular cones can be more or less harmless or dangerous according to the nature of its contents, and a toxic factor can be added to the mechanical element. A purely mechanical oedema can be re-absorbed rapidly and will produce a transitory metamorphoma; the other type of oedema, toxic in character, permanently injures the macular cones after having broken up their regular arrangements: in this case the metamorphoma becomes an absolute scotoma.

The pathological fluid can also arise more directly from the pigmentary epithelium itself, which Magitot considers to be a secretory organ, the activity of which, nevertheless, is also conditioned by the chorio-capillary circulation. Perhaps the senile hyaline secretion (Magitot) of the pigment epithelium also plays a role in the disturbance of the macular cones.

Finally, the fluid responsible for a metamorphoma could also be extravasated blood, once again coming from the chorio-capillaris. We are aware of the frequency of deep haemorrhages during the ophthalmoscopic progress of senile and myopic maculopathies. We know also that a choroidal haemorrhage is far more dangerous to the visual function than a true retinal haemorrhage because in the deeper layers the sensory cells themselves are bathed in blood.

In addition to the "fluid" factor and in connection with it, one must bear in mind the sclerotic changes and hyaline degeneration of the chorio-capillaris: the vessel walls become thickened and their lumen narrowed, and to compensate for this other capillaries are dilated. Often there is a general condition of pre-capillary spasm. In these conditions it is not surprising that the sensory epithelium of the retina becomes disorganized; this disorganization becomes apparent in metamorphomata.

Let us now turn to the structural basis of the purely central translucid scotoma, that is to say, a scotoma without metamorphoma such as may appear at the very beginning of certain maculopathies.

Once again it is an oedema, localized this time not in the deep perceptual layers of the retina (where it would displace the cones) but in the conducting layers the structure of which at the macula is so highly specialized. Duke-Elder (1940) points out clearly that "the structure of the thick fibre-layer of Henle, with its ability to swell, can absorb large quantities of fluid". It is this oedema situated in front of the sensory layer of the retina which appears to the patient as a veil or mist in front of his eyes and which he tries to get rid of by rubbing them.

In the origin of this oedema it is the circulatory system of the cerebral layers of the retina, the system of the arteria centralis retinae, which plays the great part. In point of fact, a central translucid scotoma is only rarely encountered in the early stages of myopic maculopathy, but as a rule is the precursor of the macular lesion in those retinopathies which one knows to involve the cerebral layers of the retina, of which malignant hypertensive retinopathy is a prototype. Here, also, the oedema can be more or less mechanical, "circulatory", and harmless to the retinal fibres, or, on the contrary, exudative, "inflammatory", and toxic in nature, bringing in its train irreversible disturbances of conduction.

The formation of the oedema here also is linked with circulatory disturbances due to arteriolosclerosis, which is often accentuated by a spastic condition of the retinal pre-capillaries, seen by the ophthalmoscope. I attribute a localizing significance to the two symptoms we have been discussing—pure metamorphoma and pure translucid scotoma. Each tells us in which part of the macula the disease begins, whether it is in the deep sensory complex lying on the nutritive chorio-capillaris, or in the superficial conducting part of the retina, the layer of Henle. The fact that sooner or later the patient experiences metamorphomata and scotomata simultaneously shows us that the two stages of the disease—the two areas of oedema and structural change soon merge—so that they involve all the tissues of the macula.

The macula is not only a tenuous part of the retina, but is itself an entity consisting of two parts, the deeper which is choroidal and shares pathological changes with the choroid, and the more superficial which is entirely retinal. Ophthalmoscopically, these two parts of the macula and their diseases are distinguished from each other by a very important element: the pigment.

In all deep maculopathies which from the onset give rise to metamorphomata, the ophthalmoscope sooner or later demonstrates irregularities of pigmentation; these are often very slight—at the beginning a hardly perceptible scattering which is not demonstrable in red-free light—but they are shown up by a concentrated beam of the usual ophthalmoscopic light focused a little to the side of the suspected region. On the other hand, in th

maculopathies affecting the cerebral layers of the retina there is no pigmentary disturbance. The pathological process lies anterior to the perceptual layers of the retina, in the conducting layers. The integrity of the sensory epithelium shows itself functionally by the absence of metamorphoma and ophthalmoscopically by the absence of pigmentary changes.

One more important functional symptom of maculopathy is the absolute scotoma. I have not mentioned it until now because an absolute scotoma is not an early symptom, but a final one which results from the destruction and death either of the perceptual retinal elements or of the conducting fibres. It is true that, in the relatively early stages of myopic maculopathy, minute absolute scotomata may accompany the small broken metamorphomata which characterize the visual disturbance of high myopes. But even in this case there always is an initial stage of pure metamorphoma. On the other hand, in the spread of a cerebral retinopathy to the macula, the central translucid scotoma is usually not transformed into an absolute scotoma; for this to happen, the deep sensory retina must eventually be involved, or the oedema-fluid particularly toxic.

TREATMENT

The considerations put forward in this attempt to systematize the early functional disturbances of the macula, may appear somewhat hypothetical and speculative. They have been suggested by experiments with the grid and clinical experience over some 25 years. It is hoped to stimulate renewed interest in the early qualitative alterations in central vision, because the diagnosis of a very early functional symptom at a stage before the appearance of the first ophthalmoscopic changes presents therapeutic opportunities which no longer exist when a destructive lesion has become established. Metamorphoma and relative scotoma, the initial functional symptoms of the maculopathies are, in fact, often reversible, and may diminish or even disappear with appropriate treatment.

REST.—The treatment to be put into effect as soon as a functional disturbance symptomatic of a maculopathy is diagnosed must, above all, ensure complete rest for the affected macula.

To understand this fundamental necessity, we must try to picture in all their complexity the biochemical changes and bioelectrical reactions which take place in the functionally active retina and especially in the macula which is so highly differentiated.

To rest the macula means a prolonged cessation of all visual activity and the protection of the eyes from bright light: this is not at all easily acceptable to a man or woman who is suddenly afflicted in the height of a full professional life by a visual disturbance still slight in degree and affecting one eye only, but the patient must understand the importance of an early and drastic treatment designed to be abortive in the eye already affected and preventive in the other eye.

This therapy by ocular rest is certainly more easily obtained in the discipline of the hospital than in the home. In hospital, resting the eyes can form part of a general therapeutic plan of rest, for such patients are usually overworked; the diet can be supervised, the use of alcohol and tobacco controlled and restrained, and above all psychotherapy can be put into practice. Often, however, circumstances force us to begin treatment while the patient is ambulatory, and this continues until the patient himself notices that his condition is deteriorating and becomes aware of the necessity of hospital treatment.

GENERAL PHYSICAL EXAMINATION.—Whether it is a myopic or senile maculopathy that is beginning, it is essential for the patient to undergo a general examination, particularly from the cardiovascular point of view. Special attention must be paid to the peripheral vessels and to any abnormalities in the capillary circulation. A search must be made for foci of infection, and if found, they should be treated radically.

DRUGS.—Treatment by drugs should follow our present concepts of the physiology and pathology of the capillary circulation; for these we are indebted in the first place to the classical work of Bailliart, beyond which we resort to empirical measures.

Vasodilators.—Our principal therapeutic agent, which is directed against the spasm and obstruction of the smaller vessels which bring about and dominate the pathological condition of the macula, includes all the various vasodilators at our disposal. Primarily, these are acetylcholine, a hormone, and nicotinic acid, a vitamin of the B group, and their derivatives under whatever pharmacological name they may masquerade. “Ronicol”, for example (a Roche preparation) contains as its active principle, B.pyridycarbinol, an equivalent of nicotinic acid, 25 mg. per tablet.

In the case of an incipient maculopathy, the vasodilators are only very rarely given by local injection or in massive doses (such as would be given to relieve an acute spasm of the central retinal artery); they are given by mouth in relatively small doses repeated over a very long period. Thus we order 2 to 3 tablets of Ronicol to be taken daily for a period of 8 to 10 days. After this we give a suppository containing 0.2 acetylcholine each evening for 4 to 5 days. Then again Ronicol followed by acetylcholine and so on. It goes without saying that the two drugs can be given at the same time or in another rhythm or in combination with some other vasodilator, such as Priscol (Ciba).

In addition to these known vasodilators a classical lotion is prescribed, potassium iodide 1 per cent. (Jean-Gallois, 1952). We prescribe regularly sodium iodide 1 per cent. and calcium chlorate 1 per cent., instilled daily or twice daily, and continued over a considerable time. Short waves can also contribute by producing a hyperaemia of the ischaemic macula.

The effects of these therapeutic measures cannot be observed by the

ophthalmoscope; it is the patient who will indicate on our grid the changes which occur in his metamorphomata or translucid scotomata. The functional criteria matter more than the ophthalmoscopic. And even if there is a macular lesion to be seen, the subjective indications of the patient, provided they are in the slightest degree precise, tell us far more about the effect of our therapy than the ophthalmoscopic picture, which seems often to be stationary.

Anti-exudatives.—As soon as the maculopathy shows itself by a central micropsia or a central translucid scotoma—two symptoms of oedema, accompanied sometimes in their early stages by the minute ophthalmoscopic sign of the disappearance of the foveolar reflex—we must begin a treatment aimed at diminishing the permeability of the capillary walls and aiding the resorption of the extravasated interstitial fluid.

Injections.—It is here that calcium given by intravenous or intramuscular injection may prove of value. We must remember, however, that the effect of calcium does not last more than 2 hours, a fact demonstrated by our work on the fluorescein-test in man. Injections should therefore be given right away and repeated morning and evening over many days and in rather strong doses (10-20 ml. of a 10 per cent. solution intravenously, or 10-20 ml. of a 20 per cent. solution intramuscularly).

Another drug which may perhaps help even in advanced cases of macular oedema as a retrobulbar injection is atropine (Bangerter, 1945). A 1 per cent. solution of atropine is injected 2 to 3 times a week in increasing doses from 0.3 to 0.6 ml. and up to twelve injections.

This treatment by retrobulbar injection brings me to the discussion of local therapy in general. Myopic maculopathy and senile maculopathy in all its forms are spontaneously progressive diseases. If they are taken in hand at the beginning, as we can do with our accurate method of examination, these diseases, though they cannot always be cured, can at least be improved or arrested for a time. This does not mean that our treatment always achieves these results. The disease can progress, the metamorphoma spread, or the scotoma thicken, in spite of all our therapeutic efforts. It can thus happen that our patient becomes aware of a deterioration of vision following, for example, a subconjunctival or retrobulbar injection. From then on, his reasoning *post hoc propter hoc* can make him refuse, perhaps regrettably for ever, the continuation or resumption of any further local treatment. It is unwise to discount this psychological factor, and it is therefore better to begin with extra-ocular medicaments (if I may call them this), to which no harmful effect can be attributed in case of an aggravation of symptoms during the first phase of the treatment.

Vitamins.—If a maculopathy occurs in a patient who has a tendency to haemorrhages, whether from fragility of the capillaries or delayed blood coagulation, recourse should be made to appropriate remedies: Rutine and

Vasorutine, which are the fashion to-day but whose mode of action (reinforcement of the capillary walls?) and efficacy, as you know, are in dispute, vitamin C, vitamin K, calcium, Adrenoxyl, and so on.

A popular belief opens up the possibilities of another therapeutic field. With us carrot juice is popularly believed to improve weak sight, and in recent years many of our patients have affirmed good effects from fresh carrot juice taken each morning. This empirical remedy merits serious consideration of the possible value to the retina of vitamin A, the "vitamin of the eye" *par excellence*, which is essential to the metabolism of visual purple, and which, according to recent research, is found not only in the rods but also in the cones, and particularly in the specialized sensory elements of the fovea.

Consequently it can be recommended at the onset of a maculopathy with metamorphomata localized to the physiological couple sensory epithelium and pigment epithelium, to prescribe a vitamin preparation such as "Arovit" (Roche), for example, in doses of two or three pills of 50,000 international units daily.

But it is not vitamin A alone which is important in the early treatment of maculopathy. Vitamin B₁, aneurine, which activates the metabolism of glucose and increases the oxygen consumption of the cell; Vitamin B₂, riboflavine, which enters into the formation of the enzyme of the yellow ferment of cellular oxydation and which has been found abundantly in the visual cells and pigmentary epithelium, and above all vitamin C, ascorbic acid, an important factor in cellular oxydation and reduction and also in the nutrition of the capillary endothelium—all these vitamins play a definite or at least an accessory role in our macular therapy.

There are preparations containing all these vitamins, such as, for example, "Protovit" (Roche) or "Nestrovit" (Roche) which simplify vitamin treatment considerably.

TISSUE THERAPY.—The last therapeutic measure to be discussed is very complex in nature and obscure in its action: the placenta, placental extract, and placental blood serum.

The tissue-therapy of Filatov, already 20 years old, has its greatest indication in pigmentary degeneration of the retina. All who have a personal experience of this treatment have seen, as I have, some slight functional successes and many failures. In our clinic at Zürich only a few young patients reacted favourably, in whom the tapeto-retinal degeneration was not too advanced and which still showed signs of deterioration. This evidence encouraged us to use tissue-therapy at the beginning of maculopathy and before an irreversible lesion occurred in the central chorio-retina.

How does the placenta implanted or injected under the conjunctiva act? What are the active elements? Are they the "biogenic stimulines" of Filatov liberated by a dead tissue? Are they the various and many hormones of the placenta and the serum of fresh placental blood, as we use it ourselves? Is it just simply the hyperaemia and vasodilatation caused by the implantation or the injection which causes a therapeutic effect?

It is impossible so far to reply to these questions. Whatever the answer may be, it is sufficient for the present that there is a probable or possible stimulatory action on the retina, which is worth considering also as a therapeutic agent for the circulatory and trophic disturbances which occur so frequently and are so serious in the maculopathies of myopia and old age.

Vasodilators, anti-exudatives and re-absorbents, anti-haemorrhagics, vitamins, and hormones—here is a well-stocked therapeutic arsenal. But once again, what can all these arms do against a spot of Fuchs, a disc of Junius-Kuhnt? There is nothing more disillusioning than an established macular lesion

IMPORTANCE OF EARLY DIAGNOSIS AND TREATMENT

But every maculopathy has a beginning. It is this beginning which the patient sees and experiences. It is this beginning which we can record on the functional level of symptoms which are susceptible to treatment. Let us imagine the dismay of a man who is beginning to lose his central vision and to suspect with anxiety what the future has in store for him, and is told that “the early detection of macular degenerations is not of great importance, as we can do nothing for them” (Zentmayer, 1938).

On the other hand if he were told: “we are going to endeavour to remedy your ocular disease at the very onset, and, though unable to promise you anything for certain, we are going to try every method we know to improve your capillary circulation and to rest, protect, and nourish your retina”, he would be happy. And grateful, even if he saw his doctor groping in his choice of drug or combination of drugs to which the retina would respond; grateful even if the therapeutic effect did not last . . .; grateful for his doctor's perseverance at least in trying.

To conclude, the opposite proposition may be affirmed: “The early detection of macular degenerations is of great importance, as we can do something for them”.

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