this necessary in those myopes who accept a lens of higher power than their refraction would warrant, or would accept it on a subjective test. In some cases it may be necessary to use atropine for a fortnight, in order to get full relaxation of accommodation.

(2) In pseudo-myopia the vision may be variable.

(3) That investigation of the myopes in a school for the partially-sighted along the lines suggested might be profitable and might throw some light on the nature and treatment of myopia in the adolescent.

(4) That in those cases in which there are symptoms or signs suggesting the need for orthoptic training, the presence of myopia is not necessarily a contra-indication.

(5) That pseudo-myopia is possibly more common than previously supposed, and that it occurs in adults as well as in young people, and also in emmetropes and hypermetropes as well as in myopes.

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THE PROBLEMS OF GLAUCOMA*

BY

DOC. JAN VANÝSEK

HRADEC KRÁLOVĚ, Č.S.R.

THE causes of glaucoma are still unknown, in spite of the considerable progress in science and satisfactory therapeutic results. Our knowledge today is the result of the work of generations, but in spite of its great value, we are well aware that the right solution is still wanting. The theories were always arrived at correspondingly to the discoveries in the histology of experimental pathology. It is neither advisable nor possible to do justice even in brief to all the opinions which have been expressed about glaucoma or to survey them all.

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It would be a mistake to look upon glaucoma as a single entity, created only by a single and certain cause. The variety of its forms repudiates such a conception.

In accordance with the progress of science we have been forced in the last years to correct some opinions we were accustomed to. The advancing research of the vegetative nervous system, of the mid-brain centre connected with the pituitary gland and the discovery of the nocifensory system has thrown a new light on many problems. Glaucoma has already previously been compared with oedema and I agree that this comparison is justified to a great degree. I therefore think it right to call attention to the present views on oedema and to attempt to find out whether there is a parallel between oedema and glaucoma.

According to its origin we distinguish today inflammatory, cardiac, nephritic oedema and the oedema of Quincke.

One can easily find a parallel between the inflammatory oedema and glaucoma. A typical example of this group is certainly the glaucomatous iritis. Until now it has been nearly exclusively upheld that an increase of the tension arises from the blocking of the drainage system in the anterior chamber of the eye by an exudate. This is to a certain degree probable, but it has already been pointed out previously that it would not be correct to charge only this cause. Thus Schmidt-Rimpler draws attention to the fact that a great number of cases of iritis, sometimes even with a thick exudate, are not accompanied by secondary glaucoma. A good many cases have been described, where the blockage has been proved with the great probability, but on the other hand many have been recorded where this proof has been entirely absent. There is no reason why we should not think that oedema arises in the eye in the same way as anywhere else in the body. Of course, in the other parts of the body oedema is not restricted to such an extent as in the eye where the enlargement of the bulk of the tissue is limited by the relatively inelastic coat of the eyeball. If, however, the tension rises in the capillary blood vessels of the eye, followed by a speedy reduction of oxyhaemoglobin, thus causing defective oxygenation and an accumulation of metabolites, which osmotically attract water, we have also to admit a tendency towards oedema. Since the coat of the eyeball is to a very small extent elastic and therefore incapable of compensation, a greater strain is laid by such a swelling upon the drainage of the aqueous. The regulation of the increased tension by paracentesis, which is supposed to remove the exudate which is the cause of the blockage, is often quoted in support of the opinion that the iridocyclitic glaucoma is caused by blockage of the ducts with exudate (Schieck). At

the same time it is of course possible that paracentesis of the chamber is successful because it removes the excessive amount of metabolites. We are well aware that after the disappearance of the inflammation, *i.e.*, after the disappearance of the pathological amount of metabolites, the glaucoma disappears, as it never outlasts the inflammation, although it would be quite possible to expect the increased pressure to last longer in view of the blocking of the anterior chamber. May I add that according to my impression injections with hypertonic solutions have in such cases a relatively good effect. I have very often tried to apply in such cases not only hypertonic glucose but also hypertonic saline. On the whole I can say that it often stood the test.

Similarly, it is easy to find a parallel to cardiac oedema among diseases with increased tension of the eye, *viz.*, the typical secondary glaucoma which occurs in the case of thrombosis venae centralis retinae. The pathogenesis of this glaucoma is again explained by the blocking of the anterior chamber by the products of decomposition which arise from thrombosis. Elschning looked upon anterior synechia, which sometimes occurs, as a mechanical and non-inflammatory process, which is caused by the pressure of the swollen lens. If one can compare the glaucoma complicating blocking of the central vein with cardiac oedema, the explanation is simple. The bad circulation produces again metabolites which accumulate in the eye, attract osmotically water and cause intra-ocular oedema. According to this explanation therapeutic efforts are extremely difficult. It is natural that the main interest of this comparison is directed towards primary glaucoma.

If we want to gain from this comparison with the oedema, we must first of all look for a parallel to the oedema of Quincke. It appears namely that the allergic mechanism, which is influenced by the pituitary gland, mid-brain and the vegetative nervous system may be common to both. Glaucoma has been considered for some time as an alteration of the tone of the sympathetic system. Although it was not possible to account for all the circumstances this opinion has been maintained up to the present day. This opinion was mainly supported by the favourable effect of drugs exciting the para-sympathetic, by which it is possible to diminish the pressure in the eye. Some experiments, however, which invalidate the above mentioned doctrine, do not fit into the pattern. The results of experiments consisting in excitation of the sympathetic varied considerably and those of the treatment of glaucoma by extirpation of the sympathetic were vague. After excitation of the sympathetic, an increased pressure followed for a short period and thereafter a long lasting decrease of pressure.

After some time the pressure reverted, according to the literature, to normal or increased. The opinion that glaucoma cannot be due to tone of the sympathetic system was therefore doubted since through irritation after a transitory increase, a decrease of tension sets in. This apparently vague effect of the increased tone of the sympathetic can be easily explained. All actions of life are regulated by the tension of the sympathetic and para-sympathetic. By these actions oscillations are produced. If an increased tone of the sympathetic arises, the reaction of the para-sympathetic ensues immediately and restores balance of the vegetative system. This regulation, however, is by no means precise, and the para-sympathetic response is excessive. Until balance is regained, the oscillation of both regulating elements goes on. This oscillation can be represented by waves which die away.

The same phenomenon ensues also after subconjunctival application of adrenalin, which is a typical drug exciting the sympathetic. We know that adrenalin is a stimulus for the sympathetic, *i.e.*, a substance which the sympathetic sets free and which has its effects on the organs. In a voluminous literature we can find many statements about the effect of adrenalin on glaucoma. Adrenalin was even used successfully to decrease intra-ocular pressure. This was especially successful with glaucoma simplex. Opinions, however, about the effect of adrenalin upon glaucoma differ considerably. While it is by some recommended, others warn against its use, because it has happened that by application of adrenalin a glaucomatous attack has been produced (Imre, Jess, MacCallan, Parsons, Gamo Pinto, Rubert and others). Here again a considerable incongruity in the effect of this substance ensues. Adrenalin works for a short period only, because of its quick decomposition. It produces an intensive mydriasis which is remarkable for its effect on the sympathetic. Adrenalin produces in addition a transitory vasoconstriction, which soon disappears and is replaced by a vasodilation. The effect on the tension of the eye varies again according to the literature. Knapp, for instance, instilled drops of adrenalin in 65 cases of primary glaucoma five times at one minute's interval. In 40 cases the tension remained unchanged, in 20 it was a little lower, and in 5 cases higher. I think that these incongruities in the effect of adrenalin can be easily accounted for. I therefore measured the tension every thirty seconds in 22 cases after subconjunctival injection of adrenalin. In 17 cases I found with certainty a slight but transitory increase of tension, which was immediately followed by a decrease. In one case the tension was increased for a period of three minutes, then it returned to normal. The remaining 4 cases did not show any measurable change in the way of increase, but after about two minutes a

slight decrease of tension ensued. With regard to the above mentioned measurements it is probable, that adrenalin, working only for a short period, increases the tension of the eye at first and thus provokes a reaction of the para-sympathetic, which endeavours to regain the vegetative balance and thus reduces the tension quite considerably.

Such an effect of adrenalin presupposes a normal reaction of the para-sympathetic. This might even be the reason why adrenalin provoked in some cases of inflammatory glaucoma an increased tension. I observed the tension in 6 cases, where the eye was atropinised. After a short increase in tension in 5 cases, it returned to normal. In one case I did not succeed in recording a change. In view of the small number of measured cases I cannot draw any conclusions.

It was formerly objected to the sympathetic theory of glaucoma, that glaucoma is not in any way affected by the cutting of the sympathetic. Roszin proved in 1926-27 that adrenalin has a great effect on the eye even after the cutting of the sympathetic.

It is, however, possible to object that it is not probable that the tone of the sympathetic caused by adrenalin is actually the cause for a state which is characterized by such remarkable symptoms. I am going to make use of a recent invention. As I mentioned before, adrenalin causes a transitory vaso-constriction of the blood vessel, which quickly disappears and is replaced by vaso-dilatation. Vaso-constriction can, however, be prolonged by adding thyroxin. The effect of adrenalin can be accentuated by thyroxin. We can therefore assume an accentuation of the tone of the sympathetic owing to various hormonal causes which influence the vegetative centres. It is known today that the effect of adrenalin can be accentuated not only by thyroxin, but we also know that the parahormone and the hormones of the basophilic cells of pituitary glands are especially closely connected with the sympathetic system. Insulin and the assumed hormone of the thymus are especially closely connected with the para-sympathetic system.

A series of articles describes the relation of glaucoma to the thyrotoxicoses. The occurrence of glaucoma in connection with Basedow's illness is no rarity. Hyperpara-thyroses are of course very rare and it is difficult to prove this theoretical conclusion by practical experience. In this connection Csapody's case only can be quoted, who observed an increased tension in connection with the pathological fragility of the bones with blue sclerotics.

In the case of basophilic adenoma or of hyperplasia of the basophilic cells of the anterior lobe hypertension of the eye has been observed (Dérer and Kopf, Tatár, Grosz).

Insulin has the opposite effect. Acardi, Ascher, Kadlicky, Westergaard and others report its effect in lowering the tension.

I have mentioned above that it would be possible to explain cases where glaucoma after the injection of adrenalin was brought about as a result of the non-functioning of the para-sympathetic. This non-functioning of the para-sympathetic is most likely caused, according to our yet incomplete knowledge, through the activity or rather inactivity of the mid-brain. The centres of the mid-brain are specially para-sympathetic. Their damping can be effected by mental shock, by conditioned reflexes, by degenerative diencephaloses or by inflammatory diencephalites.

Also it is possible to look for a causal connection with the glaucoma. We know, how often an attack of acute glaucoma (*i.e.*, a glaucoma where adrenalin by experience cannot be applied) occurs after excitement. It may therefore be assumed that the vegetative imbalance was further increased by the damping of para-sympathetic centres of the midbrain.

The vegetative regulation can never be represented by a straight line, but it can be best shown by a wavy line with a regular rhythm. There is a parallelism between this rhythm and that of day and night. The sympathetic has a prominent katabolic effect and incites the organism to increased activity. The sympathetic is preponderant during the day. Para-sympathetic with acetylcholine, which is its nervous stimulus, controls the anabolic actions, *i.e.*, the processes of restitution. The para-sympathetic reigns at night. In addition to this long wave rhythm there is a small oscillation in a short wave rhythm. The tension in glaucoma simplex is according to our experience and the literature greatest in the morning hours and slightest in the evening. The tension is therefore greatest at the time when the sympathetic starts its work, and smallest when the para-sympathetic begins to work. The night-morning start of the sympathetic is of course counterbalanced by the para-sympathetic which tends to reduce the tension during the day to normal. During the day it works the other way round. The course of the tension between those two points of this recurring rhythm depends on the continuous compensating effect of both constituents, which try to keep a balance. In the aetiology of glaucoma mere mechanical moments play their important part as well, mainly anatomical obstacles of drainage proved by histological examinations.

With all these interconnections I have tried to prove, though incompletely, the parallel between glaucoma and oedema. Apparently it most resembles the oedema of Quinke.

To this attempt to explain glaucoma may I add briefly the therapeutic results, most of which are of course not novel. In a conservative way it is possible to control glaucoma as follows :

1. The restoring of the vegetative imbalance

(a) raising the tone of the para-sympathetic (pilocarpine, physostigmine) blocking the choline esters for a short period, the new American DPF (di-isopropylfluorophosphate) working by the same mechanism, but for a longer period and a series of drugs related to acetylcholine.

(b) paralysing the sympathetic (this our present pharmacological explanation). Ergotamin has been used and I myself tried to use benzodioxan, but the effect of these drugs was not remarkable, it only increased the effects of miotics.

(c) Vegetative imbalance can also be adjusted with shocks. Moretты compensated glaucoma with autohaemotherapy. I myself often lowered the tension of the eye during an attack for 5-24 hours by a subconjunctival injection of the serum of the patient's blood. Stánsnik compensated the glaucoma with histamin. These slight successes could justify the opinion that some glaucomas arise on an allergic basis.

2. Removing accentuating causes (I succeeded recently in compensating two glaucomas accompanied at the same time by thyrotoxicosis only, after having administered pilocarpine with vitamin A, which is the antagonist of thyroxin). It would be probably right to look in all cases of glaucomas for the accentuating cause. Where, however, the accentuating cause is merely anatomical, a conservative therapy would only succeed to a minor degree.

In this article I wished to apply some of our knowledge about oedema to the problems of glaucoma. I am well aware that many assumptions without much proof have been expressed. It appeared to me, however, that from the point of view of these new opinions many problems are identical or overlapping.

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