Summary

Gutmann's piezometer, an apparatus for measuring the displaceability of the eyeball into the orbit, may be used with success in the diagnosing of retrobulbar tumours. I examined one case of orbital gumma with the piezometer during the course of the affection and found that the displaceability of the globe into the orbit diminished during the healing of an orbital gumma and remained later permanently less than normal. Diminishing piezometer values during the course of an antisyphilitic cure indicate resorption and cicatrization of the pathological retrobulbar process, as expressed in the form of a fibrous induration, and contribute to the diagnosis of syphilis.

LITERATURE

- Birch-Hirschfeld.—Die Krankheiten der Orbita. *Handb. d. Augenheilk.*, v. Graefe-Saemisch, 2 Aufl., 1909.
 ——— Die Krankheiten der Orbita. *Handb. d. Ophthal.*, by Schieck Brückner, Bd. III, 1930.
 Gutmann, A.—*Trans. Ophthal. Soc. U.K.*, Vol. LIV, 1934.
 Freyler, H.—Erfahrungen mit dem Piezometer von Gutmann. *Zeitschr. f. Augenheilk.*, Bd. LXXXII, p. 127, 1933.
 Gutmann, A.—Piezometer zur Diagnostick retrobulbärer Orbitalgeschwülste. *Zeitschr. f. Augenheilk.*, Bd. LXIII, p. 136, 1927.
 Hirata, Z.—Ein Fall von Orbitalgumma, welcher bei der Untersuchung eine besondere Schwierigkeit bot. *Jap. Ref. Zentralbl. f. d. ges. Ophthal.*, Bd. XXV, p. 155.
 Igersheimer.—Syphilis und Auge. 2 Aufl., p. 444, 1928.
 Larrichia, E.—Entwicklung eines Kleingummas innarhalb der Augenhöhle. *Ann. di Ottal.*, Vol. LVII, p. 198; Ref. *Zentralbl. f. d. ges. Ophthal.*, Bd. XXII, p. 195, 1929.
 Meller.—*Zeitschr. f. Augenheilk.*, Bd. LXXX, p. 112, 1933.
 Raffin, A.—Ueber orbitale Syphilis. *Klin. Monatsbl. f. Augenheilk.*, Bd. LXVI, p. 147, 1921.
 Werner.—Ueber syphilitische Gummabildung der Orbita. *Inaug. Diss.*, Jena, 1913.

SOME REMARKS ON OEDEMA

BY

J. A. VAN HEUVEN

UTRECHT

ALONG various roads attempts have been made to approach the origin and nature of inflammations. These investigations were often made in what might be called a "static" way, *i.e.*, an existing inflammation was thoroughly studied. That this manner of investigation was used so frequently may be due to the fact that in the days in which these problems were acute, not many other ways were available. Thus minute descriptions have been

given of the conditions which existed at a certain moment. One never sees what happens, only what has happened.

Now it seems attractive to follow a "dynamic" way, and after having produced an inflammation, to watch its course closely. At the same time an attempt should be made to understand something of the cause of what is happening.

Now inflammations may be produced in an endogenic and in an exogenic way. As a matter of fact all the inflammations of the eye can be grouped under these two headings. In experimental work the most preferable method is the exogenic one, and especially one of a non-bacteriological nature. I have been on the outlook for a substance by means of which it would be possible to produce an inflammation of practically always the same intensity. Making use of the experience gained in this field by Chiari and Januschke, I presently obtained satisfactory results with oleum sinapis. Oleum sinapis represents a group of substances which are able to produce inflammation, attended with chemosis. This chemosis dominates the clinical picture.

If one takes a rabbit and instills into its conjunctival sac some drops of oleum sinapis, one is able to watch closely the beginning of an inflammation by means of the slit-lamp. As a matter of fact besides a change in the circulation and later on a chemosis not

Conjunctiva (normal) of rabbit after intravenous injection of trypanflavin.

much else can be seen. The concentration and quantity of the drops merely influence the rate in which the symptoms arise.

Now the changes in the circulation which arise consist of a hyperaemia, a pericorneal injection and a widening of the pericorneal vessels. There is no disengagement of water from the

vessels to be seen. The problem of the origin of chemosis therefore cannot be solved by direct inspection.

Nor did previous research work, whether of anatomical (Wessely) or of a chemical nature bring any definite solution. The most remarkable thing which happens is the arising of chemosis. This chemosis shows a peculiar picture, one might assume that just as in the case of oedema, liquids had penetrated into the tissues. It appears however impossible to get hold of liquid whether by means of puncture or by incision, and even squeezing fails.

These phenomena appear to be analogous to those which may be obtained by injecting some liquid under the conjunctiva; one can never recover it, it has become incorporated with the surrounding tissue.

In the following experiments a different scheme has been followed namely that of vital-staining. In doing vital-staining and following the technique of Knussel and Vonwiller, one needs liquids of a concentration of at least 1 per cent. These solutions are strong enough to cause destruction of the tissues and in doing so, to change the picture entirely.

It was chiefly for this reason that I preferred to inject the staining matter directly into the blood of the rabbit, using for this purpose one of the veins of the ear. In this case good results may be obtained with much weaker concentrations, so that there is no danger of the structure of the tissues being changed. Moreover it has the great advantage of giving us an opportunity to watch the gradual appearance of the colour in the blood.

It is now possible to use liquids in very weak concentrations. I made use of solutions of fluorescein and of trypaflavin. Now fluorescein can be seen in a concentration of $1/800,000,000$, and trypaflavin in a concentration of $1/1,000,000,000$. The fluorescein is of course only visible if a source of light is used, which contains a good deal of ultra-violet light.

An arc-light was used with effect carbon points, a circuit of 6 amp. quartz glasses and Uvet filters.

The conjunctiva of a normal rabbit was studied in this light by means of a slit-lamp. Then an intravenous injection was made in the ear of the animal with fluorescein, 40 m.g. pro kilo. weight. Now the blood vessel can be seen beautifully by fluorescence. An appearance of the colour from these vessels cannot be seen. It seems however that there is a kind of coloured cylinder round the vessels. If one now produces a chemosis by the instillation of some drops of oleum sinapis, no change in this picture can be observed.

Using trypaflavin instead of fluorescein one gets quite different results. If one takes a rabbit with normal conjunctivae and injects into one of the veins of its ear a solution of trypaflavin containing

30 m.g. pro kilo. no fluorescence of the blood's vessels is to be seen. A kind of meshwork however may be observed which previously could not be seen, which shows no connections with the blood vessels (see illustration). After instillation of oleum sinapis into the conjunctival sac this meshwork now becomes so plain that it can be seen macroscopically, if examined in ultra-violet light. It is impossible to see any liquid appearing from the blood vessels or to discover any connection between the blood vessels and this meshwork. The more pronounced the chemosis becomes the plainer this meshwork becomes and when the chemosis disappears again the meshwork also disappears. One gets the impression that it lasts a little longer than the chemosis.

From these experiments it appears that in inflammations the normal circulation of the blood is disturbed. This may be observed without vital staining and is in agreement with what has been written by various authors. The vital staining, however, also reveals a change in the circulation of the lymph. The nature of this change is opposite to that of the blood circulation. In vital staining, however, we see an increase in the afferent current, while the former shows an increase in the efferent current. This is evident from the fact that on the increase of the chemosis the lymph vessels become clearly visible. Now in inflammation there happens to be an increase in the permeability of the vessels. This causes liquid to leave the vessels; and this liquid appears incapable of re-entering them. It is through the lymph vessels that this liquid leaves the tissues again. Now the capacity of the lymph vessels appears to be insufficient to digest the total supply at once and this causes the clinical picture of the chemosis.

Two questions arise: Firstly. Where does the tryptaflavin remain from the moment it leaves the blood vessels until the moment it becomes visible in the lymph vessels? It must be in the tissues between these vessels and in a very strongly diluted condition. Firstly pro time unit only a small quantity leaves the vessels, this is spread in the tissues. Now the question arises: "By what power is the tryptaflavin moved into the direction of the lymph vessels?" Apparently by a property which is shown by the tryptaflavin and not by fluorescein. And this leads up to the second question: "Why can the lymph vessels be observed after injection of tryptaflavin and not after an injection of fluorescein?"

From the experiments of F. P. Fischer, Witgenstein and Krebs, Witgenstein and Gaedertz, Ellinger and Hirt it is known that in the blood fluorescein is charged positively and tryptaflavin negatively. This implies that they are attracted c.q. repelled by tissues, having an opposite, resp. equal charge. From the experiments of Nistler it is known that lymph vessels are positively charged. I think that this can explain satisfactorily the tendency

on the part of the tryptaflavin to move into the direction of the lymph vessels and also why there is not such a thing in the case of fluorescein. Not much has been written about the lymph vessels of the conjunctiva. There is just one paper by Knüssel and Vonwiller, who succeeded in making the lymph vessels visible by staining with kresyviolet. This stain is also charged negatively in the blood. Furthermore Cuénod and Nataf (*Bull. Soc. d' Ophtal. de France*, 1934) show a picture which is also from Knüssel and Vonwiller in which some lymph vessels can be seen which are similar to those mentioned above. The method described in this paper is much more sensitive than any used previously.

THE CLINICAL VALUE OF TRYPTOPHANE-REACTION

BY

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UTRECHT

A NUMBER of papers on the importance of the tryptophane-reaction in the diagnosis of meningitis tuberculosa has lately been published in various medical journals. A list of these papers was drawn up at the close of an article in the *Zeitschr. f. Kinderheilk.*, Bd. LVI, Hft. 6, 1934, by H. M. Schumacher, who concluded that in every case of meningitis tuberculosa the reaction is positive, whereas it is invariably negative in any other case in which the liquor is not very cloudy or bloody or purulent.

In view of the close affinity between aqueous and liquor cerebri it would seem interesting to trace the course of this reaction on the aqueous in cases of ophthalmic tuberculosis, especially as a reaction quickly showing whether a process is of a tuberculous nature or not, would surely be useful for clinical purposes.

The tryptophane reaction is a simple one and does not present any serious practical difficulties; but ophthalmologists are a ways somewhat hampered by the exiguous quantity of the material available. Consequently in the first place it was necessary to ascertain whether the reaction could still be performed with a quantity of liquid of not more than 0.1 c.c. This limit has been set, as puncture of the anterior chamber always yields this minimum quantity. In the second place the degree of sensitiveness of the reaction must be made sure of, and therefore various solutions of pure tryptophane