ANGIOMATOSIS RETINAE, ELEVEN YEARS AFTER DIATHERMY COAGULATION

BY *Derrick Vail*, M.D.*

Presumably every ophthalmologist, neurologist, and neurologic surgeon is by now thoroughly familiar with the disease known as angiomatosis retinae (von Hippel's disease) and the commonly associated concomitant angiomas in the neurologic and occasionally visceral structures, described by Lindau (1924). The conjoint form, von Hippel–Lindau's disease, is a fascinating group of cases that are probably not nearly so rare as a survey of the literature indicates. When a clinical disease entity becomes firmly established in medicine, many cases of it are not reported in the literature unless there are unusual or atypical features.

Our ophthalmic textbooks have excellent chapters on the disease (Duke-Elder, Elwyn, Reese, Troncosco, Walsh, to name a few). Special articles are numerous (one of the best being that by Rados). It is therefore unnecessary to preface this contribution with a repetition of what is already so well known.

Although this paper is devoted primarily to a discussion of the treatment of the disease in the eye, especially by diathermy coagulation, there are however a few general items of interest that should be added. According to Duke-Elder, the first case to be reported was that of Panas and Remy (1879), followed by Fuchs (1882), Lagleyze (1884), Darier (1890), Wood (1892), Treacher Collins (1894), and Von Hippel (1895, 1903), who established it as a clinical entity in 1904. To this list of pioneers in the subject should be added the name of Galezowski, whose *Atlas of Ophthalmoscopy* was published by Balliere in Paris in 1886. Professor E. B. Streiff has recently drawn this to our attention by finding that Plate 28, Figure One, is a classic painting of the disease. Furthermore, Galezowski's patient died of a "gliosarcomatous" tumor of the brain. This is probably the first case of von Hippel–Lindau's disease on record.

There is still some confusion in the differential diagnosis, especially in the later stages of the disease. The recognition of the retinal lesions

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in the early stages presents little difficulty, for the presence of a pair of enormously dilated vessels, entering or leaving a tumor that is usually located in the far periphery and that may vary in color from white or pink to red, is too striking to miss. However, multiple congenital aneurysms may cause confusion. Here both arteries and veins may be enormous in size, but there is an absence of exudation, which is part of the von Hippel entity. Later on in the course of angiomatosis, the amount of exudation, hemorrhages, and gliosis may suggest Coats's disease, or even retinoblastoma.

A. B. Reese has succeeded fairly well in clarifying the puzzle of Coats's disease for us. He shows that this is basically a more or less masked telangiectasis of the retinal vessels, with the formation of a thick homogeneous polysaccharide basement membrane under the endothelium. This often causes atresia and occlusion of the vessels, leading to formation of new vascular channels. In turn edema and hemorrhages occur in the deeper retinal layers which lead to detachment of the retina.

Recently Renard and Brégeat have described a few cases more or less resembling angiomatosis retinae. They call these "formes frustes," and they may well be variants of the condition. These included an atypical Sturge-Weber syndrome, with its variations, and the Syndrome of Bonnet, Dechaume, and Blanc (circoid aneurysms of the retina associated with intracranial and facial circoid aneurysms), as well as a number of cases of isolated dilated and tortuous vessels, usually venous, sometimes associated with a "glial" plaque.

In the evolution of angiomatosis retinae it is convenient to separate the cases into four stages:

Stage I. Arterial and venous dilatation, followed by the formation of the angioma. May be single or multiple.

Stage II. Retinal hemorrhages and lipoid exudates producing star-shaped figures or retinitis circinata (concavity usually towards the angioma).

Stage III. Massive exudation and retinal detachment.

Stage IV. Absolute glaucoma, uveitis, and loss of the eye.

There is a variable interval between stages, and, apparently, any stage may suddenly and without much warning turn into a later one. The longest interval between stages seems to be between I and II (up to several years); the time is shorter between II and III, and shortest between III and IV.

It is interesting to note that in the cases where it is recorded, ocular tension in Stages I and II is normal, below normal in Stage III, and, of

course, markedly elevated in Stage IV. The fact that the ocular tension is normal in the first two stages of the disease perhaps weighs against the vascular theory of glaucoma.

About 20 percent of the cases of angiomatosis retinae had Lindau's disease, approximately 40 percent were bilateral, and 22 percent showed a familial history including Lindau's disease (Usher). The heredity seems to be a dominant one and not sex linked. The sex incidence is about evenly divided.

The ages of the patients varied from three to sixty years, but the average age is twenty-five. Papilledema is rare; if found, it may be intermittent and indicate some intracranial involvement. Papilledema may be found when the ocular tension is low (Stage III), and it does not necessarily indicate an elevated intracranial pressure.

Craig *et al.* said "we have encountered many cases of hemangioma of the cerebellum without angiomatosis retinae." N. L. Aronson (neurosurgeon) said, "my experience and the literature show a rare association of the two lesions. Perhaps many of the reported cases were examined only by neurologists and neurosurgeons and without the use of a cycloplegic agent. This would account for missing some of the less conspicuous peripheral lesions." Then he, perhaps somewhat ruefully, admits, "I am sure that a competent ophthalmologist can see many things a neurologist might overlook."

Likewise we ophthalmologists might admit that, judging from the cases reported by ophthalmologists, relatively few have detailed neurologic findings or even a mention of the fact that the patient was examined by a neurologist or neurosurgeon. So it is a case of faulty teamwork on both sides. If this were corrected it might well turn out that the incidence of the conjoint disease is much higher than the 20 percent figure cited above.

CASE REPORT

My interest in the subject was sharply focused when on May 21, 1946, I saw a patient who had a typical angioma in the left eye. She was white, aged forty, and complained of failing vision in each eye for the last year and a half. The following notes are taken from my report of this case in 1949. Early in March, 1946, her vision in the left eye had failed perceptibly.

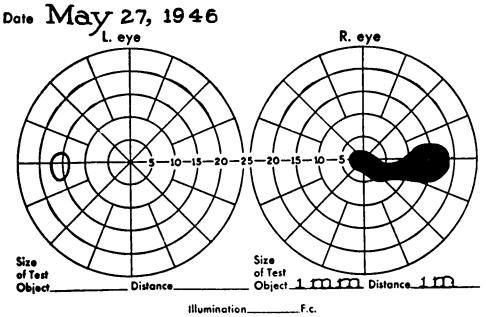
On January 24, 1945, her previous ophthalmologist had found pallor of the right optic disc and the corrected vision reduced to 20/100. The left optic disc was normal, but the vision was only 20/100. Field studies showed bilateral central scotoma, and a diagnosis of toxic amblyopia

was made. She had been a heavy user of tobacco and alcohol, did not eat properly, and was emotionally upset over an impossible domestic situation. She discontinued the use of tobacco and alcohol, was given large doses of vitamins, especially the B complex, and seven months later her vision had improved to 20/30 in the right eye and 20/25 in the left.

On February 9, 1946, the patient complained of a shadow in the upper nasal field of vision of the left eye. The vision was reduced to 20/70, and she said that her ophthalmologist reported a large "hole" in the retina surrounded by a lot of white spots in the lower outer quadrant of the left eye. Later she was told she had von Hippel's disease.

At the time of her first examination by me, the vision in the right eye with correction was 20/30—1, J2; in the left is was 20/70—. The right optic disc showed temporal pallor, and the central field a small cecocentral scotoma (Figure 1). The fundus in the left eye (Figure 2) showed a sharply defined, circular, cherry-like spot about one disc diameter in size, localized 18 mm. back from the limbus between 3:00 and 4:00 o'clock. It was surrounded by flaky patches of exudate (lipoid). The inferior temporal vein, which was three to four times its normal size and exceedingly tortuous, ran along its usual course but abruptly took a right-angle turn to plunge into the cherry-like tumor. Branches from the superior temporal vein embraced the lesion from above. Between the lesion and the fovea was a cluster of flaky white exudate patches in all of the layers of the retina, as seen with the binocular ophthalmoscope. This cluster was arranged in a semilunar manner, the concavity towards the angioma. There were minute hemorrhages above, below, and nasally to the tumor.

On June 1, 1946, under Pentothal Sodium intravenous anesthesia, the sclera over the site of the lesion between 3:00 and 4:00 o'clock was exposed and a single ignipuncture was made with a diathermy needle 1.5 mm. long (40 Ma. for 4 seconds). After ophthalmoscopic verification of the accuracy of the first puncture, seven more ignipunctures were made around it. The scleral area covered was roughly 3 mm. in diameter. Ophthalmoscopic examination showed that the involved area was "cooked," white, and edematous, so that the outline of the "cherry" could barely be seen. There was no intraocular hemorrhage. Recovery was uneventful. The vision two months later with correction was 20/30+, J1. The site of the tumor was flat, heavily scarred, and the large blood vessel coming from below was reduced to a thin grey line. There was a slow but steady decrease in the degree of lipoid retinop-



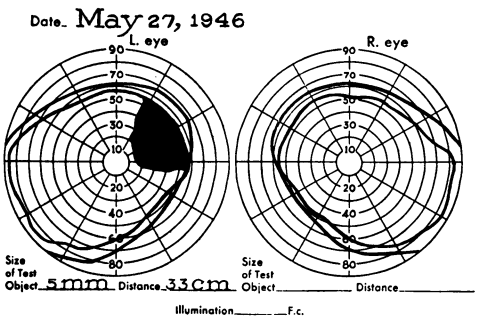


FIGURE 1. FIELDS OF VISION, MAY, 1946

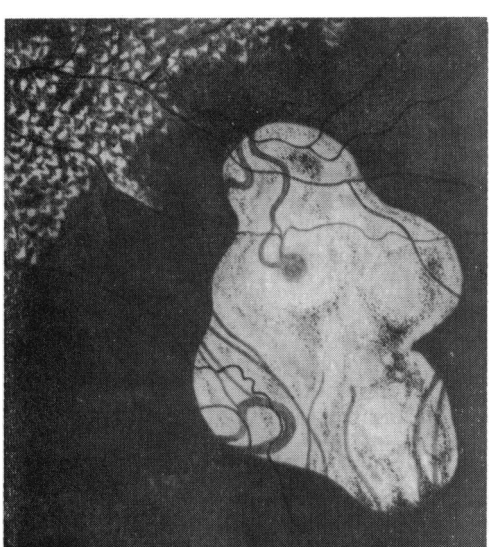


FIGURE 3. LESION THREE MONTHS AFTER DIATHERMY COAGULATION

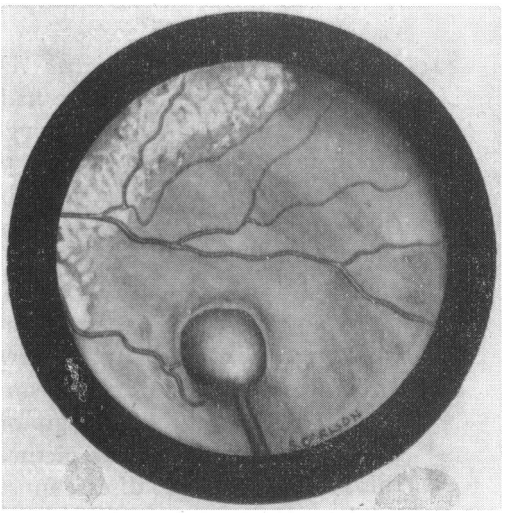


FIGURE 2. TUMOR, LARGE VESSELS, AND RETINAL LIPOID CHANGES, MAY, 1946

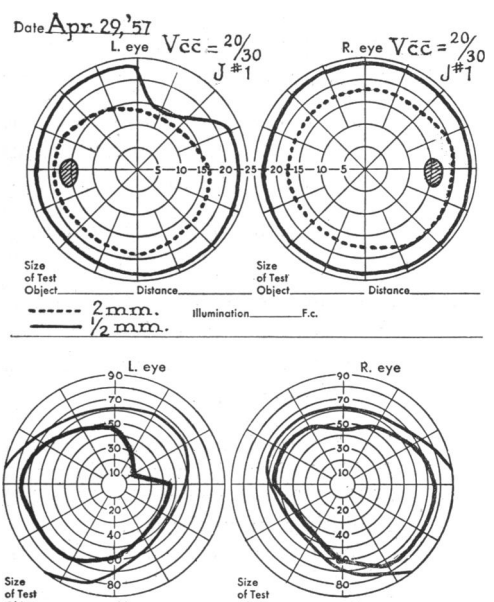


FIGURE 4. FIELDS OF VISION, APRIL, 1957

athy, but it was not until two years later that all traces of the exudate had disappeared. The scar was firm, sharply defined, outlined in pigment, and there was no elevation of the retina (Figure 3). The left vision (corrected) was 20/20—.

Neurologic and psychiatric history.—In April, 1947, the patient had a psychogenic crisis. She had been drinking heavily and showed some ataxia. Her physician thought she might have multiple sclerosis. An X ray of her skull at that time showed: ". . . a circular defect about 1 cm. in diameter located just to the right of the midline in the frontal bone. The defect communicates with the venous channel, which has no counterpart on the other side, which extends downward and slightly laterally across the frontal bone. This defect is the result of an unusually large venous channel, but it could be the result of a vascular tumor. The skull otherwise appears normal."

She was treated, however, as an alcoholic, made a splendid recovery, and all of her neurologic symptoms seem to have disappeared. There is no change in the X ray picture in her skull. Obviously, in view of this finding, Lindau's disease must ever be considered a possibility.

The most recent ocular examination of the patient was on April 29, 1957. The corrected vision in the right eye was 20/30, in the left 20/20—, and J1 in each eye. Ocular tension was 14.6 each eye. The visual fields showed no change (Figure 4). The scar in the fundus of the left eye showed slightly more pigmentation. There was no evidence of recurrence of the original angioma or the development of new ones. The fundus of the right eye was entirely normal.

The report of the neurologic examination, May 6, 1957, by Dr. Lewis J. Pollock is as follows:

> In 1947, when I first saw the patient after you had operated on her, her complaints were a feeling of insecurity, unsteadiness in gait, and a consciousness of the left leg, and more unsteadiness in that leg. She had fallen downstairs. She also had some difficulty in starting the urinary stream. At that time, there were no objective neurologic pathologic findings.
>
> In 1951, although she complained of her left foot dragging, the neurologic examination was negative.
>
> In 1954, there was definite evidence of paresis and spasticity in the left lower extremity, and subjective sensations of tingling in the upper extremities. In November of that year there was some incoordination, paresis, and ataxia of the left lower extremity. The deep reflexes were increased, and there was a Babinski sign on the left.
>
> You reported a centrally placed scotoma in the right eye and asked if this might not be the result of multiple sclerosis. It was my opinion it well might be.
>
> In January of 1955, Dr. M. H. Wald reported that she had had three exacer-

bations involving the left arm and to a lesser degree the leg, in all instances clearing up usually in from thirty-six to forty-eight hours.

Dr. Loyal Davis (neurosurgeon), in July of 1955, did not consider that the pathology warranted an exploration.

In September, 1955, she experienced an electrical shock. When she recovered from her fright, she was able to use her left hand. I saw her a week later when she again had tingling and she had a positive Hoffmann sign in the left hand and absent abdominal reflexes.

A spinal fluid examination, made by Dr. Wald before I saw her, showed a negative Kahn, a trace of proteins (Pandy) and 705 milligrams per cent chlorides.

I saw her again on May 6, 1957. She is walking with a slight hemiplegic, scuffing gait. The left nasolabial fold is deeper. There is more tone in the left sternocleidomastoid. Extraocular muscle movements are normal. There is no nystagmus. There is a slight rapid oscillatory nystagmus in the left eye looking to the left. There is a slight increase of associated movement in the right upper extremity on spreading the fingers. There is a slight falling away of the right upper extremity. There is no ataxia. The grasp is 80 kilos on the right; 50 on the left.

There is a very slight ataxia in the left lower extremity. The right Achilles' jerk is brisk. There are a few clonic movements; they are more marked on the left, but the Achilles' jerk is greater on the right. The left epipatellar jerk is greater. The wrist jerks are diminished, as are the ulnars. The right biceps is greater than the left. The left triceps is absent; the right is diminished.

There is a bilateral Babinski, right Oppenheim, right Chaddock, left Chaddock, and a left Oppenheim. The abdominals are absent. There was no loss of vibration, joint, touch or pain sense. There was no astereognosis; no aphasia; no apraxia.

The check reflexes are very slightly diminished.

The bilateral signs, urinary disturbance as well as your findings are more than suggestive of multiple sclerosis.

REVIEW OF THE LITERATURE

There are five methods advocated for the treatment of angiomatosis retinae: (1) radium (Moore), (2) roentgen radiation (Cordes *et al.*), (3) electrolysis (Neame), (4) diathermy (Weve), and (5) heliocautery (Meyer-Schwickerath). Of these methods, diathermy coagulation of the tumor or tumors has been the most popular, because of its many advantages. These are: ease of use; accurate, often pin point, destruction of the lesion; little or no damage to the unaffected parts of the eye; little delayed or remote damage to the eye; great familiarity on the part of the surgeon with instrumentation and accurate localization of the area to be treated; versatility in the use of surface coagulation as well as of penetrating ignipunctures according to indications; ophthalmoscopic observation during the procedure; no danger of producing cataract;

and, as the following analysis of cases in the literature so treated shows, remarkably good and consistent results with a high percentage of perfect cures and the disappearance of exudates. The chief danger is postoperative vitreous hemorrhage.

There are cases of cures by radium (Foster Moore *et al.*) and X rays (Cordes *et al.*) reported in the literature. One of the most striking cures of this sort is that reported by Cordes and Schwartz before this Society in 1952, when they showed a case of cure with an eleven-year follow up.

On the other hand, there are cases of primary failure with radium (Handl, Neame) and with X ray (Kent, Guyton, and McGovern), where second operations with diathermy coagulation showed five successes and one failure (Guyton and McGovern).

In addition, Ballantyne reported the histologic findings in an eye that had been treated with radon seeds (4,000r), six months later with X ray (four treatments, total 4,750r), with vision 6/60 three months later. Two years later there was sudden loss of vision due to massive hemorrhage in the vitreous, and the development of severe acute glaucoma. The histologic studies showed more destruction (hyalin degeneration) of the normal retinal vessels than of the angioma and its feeders.

A most thorough review of the literature has disclosed reports of 47 eyes (38 patients) with angiomatosis retinae that had been treated with diathermy coagulation as the definitive or final form of treatment. The youngest patient was aged seven, the oldest forty. The average age was twenty-five. There were 16 males and 13 females. The sex of the remaining 18 was not given.

The angiomas were monocular in 9 cases, 6 of these involving the left eye only, and binocular in 20. The remaining 12 cases were not specified.

Thirty-nine eyes had a single angioma, 5 eyes showed two lesions, and 3 eyes showed three or more angiomas.

Most of the lesions were in the temporal periphery (14 upper temporal, 12 lower temporal). In 8 eyes the tumors were in the nasal periphery, in 5 the lesions were directly above, and in 3, directly below. Five cases were not specified.

In ten eyes the disease was in Stage I; in 21 eyes, Stage II; in 9 eyes, Stage III; although not specified in 7, it is reasonable to assume that the disease was in the first or second stage.

Ten patients (21 percent) had a family history of von Hippel or Lindau's disease or both (Saebö and Rumbauer, especially).

Nine patients had neurologic or visceral involvement, but in more

than 50 percent of the cases surveyed there was no mention made of a neurologic examination.

The color of the tumors varied in description from grey white to cherry red, most of them were noted as reddish in color. The size varied, when mentioned, from ½ disc diameter to 3½ disc diameters. Most of the lesions were elevated, from ½ diopter to 3 diopters. The exudates were described as flaky or circinate but in only three cases were there star shaped figures in the macula.

The treatment with diathermy was completely successful in 33 eyes (70 percent). Success here means total destruction of the tumor, smooth postoperative recovery, with preservation and restoration of the preoperative vision, which was very good in the majority of the cases, especially in Stages I and II of the disease. Six eyes were improved (tumor destroyed and eyeball preserved). There were 8 failures, one of these (Saebö) appeared to be successful for four years, then the disease spread to other parts of the fundus, producing a detached retina and resulting in a failure. On the other hand it is probably not unusual for the postoperative reaction to persist for some time and only at the end of several weeks, or even months, to clear with restoration of useful vision (Lewis, Guyton, and McGovern).

Nine of the 38 patients had both eyes operated upon. Of these, 5 had a successful result in each eye and 4 a successful result in only one eye.

Seventeen eyes showed a postoperative hemorrhage in the vitreous (one on the eighth day, one on the twenty-fifth day); 5 of these were failures. Eight eyes had a temporary detachment of the retina (in 4 of these, the detachment was present before surgery). Five eyes had a permanent detachment of the retina (in 2 of these, the detachment was present before surgery). In 15 eyes the absence of a postoperative hemorrhage was definitely noted.

The period of observation of the successful cases varied from two weeks (much too short a time to be significant) to eleven years (Vail) and twelve years (Neame). The average period was less than two years.

Five eyes had multiple operations, 2 with success. One of the failures had a scleral resection. Three of the successful cases were treated with electrolysis followed by perforating diathermy. Most of them (33) had surface diathermy followed by penetrating diathermy, and 10 had penetrating diathermy alone (e.g., Vail, Straatsma, Tsao *et al.*). No cases so far as could be determined were treated by surface diathermy alone.

Most authors sought to destroy the tumor as the target of the operation. A few sought to destroy the feeders, sometimes getting into trouble.

Most of them preferred to follow Weve's advice and perform a surface diathermy coagulation, immediately followed by a few penetrating points. Weve says that in multiple tumors the whole job should not be done at once; rather the necessary operations should be spread over intervals of several weeks.

In the event that the authors gave the details of their technique, which was not frequent enough, the current used in successful cases varied from 15 to 100 Ma. for three to seven seconds. Obviously these figures are not of much value. It would appear however that a current of 100 Ma. is unnecessarily strong and brings with it definite risks of postoperative complications. The dictum used in retinal detachment surgery, to the effect that one should use the minimum amount of current that is just enough to do the job, applies here as well.

It may be fruitful to analyze some of the failures. Rumbauer, for example, reports a case in a man of twenty-seven. The right eye had been blind for a year. The left eye showed two angiomas in the temporal area. Lipoid changes were present, as well as a partial retinal detachment in the temporal periphery. Vision was 6/60. The vision on the day prior to surgery was 1/60, and the detached retina and exudate were much worse (early Stage III). Diathermy coagulation was done (50–60 Ma., 2–3 seconds) into the tumors. There was blood in the vitreous, detachment persisted. Four weeks later diathermy in the area of detachment was done. One and a half weeks later a third diathermy operation was done. It was followed later by scleral puncture below, which yielded dark blood. Vision was 2/60; then followed complete retinal detachment and failure.

Another example is a case of Saebö's. The left eye of a woman aged thirty-two had vision of 5/6. There was one angioma below. Two years later diathermy was performed, with an immediate postoperative retinal detachment and failure.

On the other hand, MacRae reported a case of two angiomas in the temporal part of the left eye of a woman, aged twenty-seven, whose right eye was totally blind. He applied catholysis (3 Ma. for 3 seconds) and surface diathermy (100 Ma. for 8 seconds), and short-needle perforation diathermy (40 Ma. for 3 seconds) to the upper angioma. Immediate postoperative edema of the retina and subhyaloid hemorrhage followed. One month later a fresh vitreous hemorrhage occurred. A second operation was performed. It consisted of surface diathermy, then catholysis (3 Ma. for 3 seconds), followed by perforating diathermy (40 Ma.); no hemorrhage occurred but much edema of the retina ensued. Two months later the lower tumor was operated upon. It was accu-

rately localized with catholysis, followed by surface coagulation and penetrating diathermy coagulation. The final vision seven months after operation was 6/18 and "steadily improving."

An analysis of the results of surgery in the different stages of the disease shows:

Stage I	10 eyes	2 failures,	1 improved
Stage II	21 eyes	3 failures,	2 improved
Stage III	9 eyes	2 failures,	3 improved
Not specified (I and II?)	7 eyes	1 failure	

It is remarkable that 4 of the 9 eyes that were operated upon in Stage III were successes (Weve, Tsao, Michaelson, Guillaumat). On the other hand, 5 failures in Stages I and II of 31 eyes is still higher than one would like. It is possible that too much was done in these cases, that too much diathermy current was used for a particular eye, or that hitting choroidal or feeder vessels resulted in severe intravitreal hemorrhage or retinal detachment. In 6 of the cases of failure, hopeless postoperative retinal detachment was responsible. There are not enough data given in the reported cases to determine with any accuracy this most important point.

There are a few additional interesting points gleaned from a study of the case reports:

1. Rumbauer includes 2 cases that were spontaneously healed (without surgery), thus showing that the prognosis is not invariably bad.

2. Tsao *et al.* noticed that "when the eyeball is pressed with the finger the tumor becomes pale." Also, that the feeding vessels showed no branches but after operation, branches appeared. The authors believe these to be old channels reopened. Furthermore, the secondary changes (lipoid exudate, and so forth) are not entirely due to the angioma but probably result from vascular malnutrition of the retina.

3. Craig *et al.* report that one of their patients had a retinal angioma that was mistaken for tuberculous focal choroiditis for some time before its proper nature was recognized.

4. Guillaumat *et al.* found that the use of steroids did not help in postoperative retinal edema.

5. Straatsma found that pressing on the globe caused pulsation of the dilated vessels, but not of the tumor.

6. Guillaumat *et al.* did the fluorescein test in one of their patients prior to surgery. It was normal, ruling out to some extent the possibility of an increased permeability of the capillaries in this disease.

7. Saebö remarks that "the situation is especially grave when the

tumor or exudative changes take place in the central part of the fundus."

8. Möller points out that fresh angioma may develop in the retina.

9. Weve optimistically says "it appears that this disease, hitherto considered incurable, gives practically 100 percent chance of cure, provided that it is recognized in time."

10. Handl remarks that he had not seen dilated episcleral blood vessel clusters lying over the area of the angioma, either in the ciliary vascular area or in the area of the vortex veins as noted by Schreck.

11. Finally, Meyer-Schwickerath, who has devised an instrument for coagulation of the retina by light, has recently reported a case of angiomatosis retinae successfully cured by means of his instrument. His illustrations show that the tumor was totally destroyed four months after treatment. Since his method is one of coagulation, his case should be included among the successes reported above.

SUMMARY AND CONCLUSIONS

1. Angiomatosis retinae (von Hippel's disease) and its systemic counterpart (Lindau's disease) are disease entities now firmly established in medicine. They are probably more common than are supposed. Neurologists and neurosurgeons may miss the ocular lesions, ophthalmologists the systemic ones. Thus teamwork is essential.

2. Angiomatosis retinae can be divided into four stages of progression during its relentless evolution. Stage I consists of one or more dilated and tortuous veins, more or less parallel, running usually to the peripheral and pre-equatorial area of the retina. They terminate in a circumscribed tumorous area (the angioma) which may be single or, much more rarely, multiple. Stage II consists of retinal hemorrhages, but especially of a deposit of flaky lipoid exudates scattered in the various layers of the retina. Stage III consists of massive exudation and retinal detachment, and Stage IV is terminal with uveitis, absolute glaucoma, and loss of the eye.

3. It seems to be a rare possibility that the disease may arrest itself at Stages I or II.

4. The disease is easy to recognize during Stages I and II, but Stage III may be confused with Coats's disease, advanced circoid aneurysm, multiple congenital aneurysms, or retinoblastoma. Like most familial and hereditary diseases, confusing "formes frustes" may be encountered.

5. Angiomas have been successfully treated by radium, X rays, catholysis, diathermy coagulation, and, most recently, by heliocautery.

6. This paper is primarily concerned with the treatment of this disease

by electrocoagulation. Forty-six such cases (38 patients) collected from a review of the literature are analyzed. To this list is added an additional case report, eleven years after successful surgery.

7. The operation successfully cured 33 (70 percent); 6 were improved (eyeball saved, poor or little vision), and 8 were complete failures.

8. Stages I and II are the most favorable for surgery, although it should be noted that 4 of the 9 eyes operated on early in Stage III are considered to be successes.

9. Mild surface diathermy coagulation followed by pin-point ignipunctures into the tumor itself seems to offer the best prospect for success. If the tumor is destroyed, the feeder vessels shrink in size and lose their tortuosity. The lipoid deposits disappear within a year thereafter. If they do not disappear, it presumably means that the tumor has not been destroyed, that others may be present, or new ones developed.

10. The greatest hazard is hemorrhage into the retina, choroid, or vitreous. For this reason diathermy should be applied with the weakest current capable of doing the job, and under frequent ophthalmoscopic control.

11. Multiple tumors are best treated separately and at intervals.

12. Sound and cogent reasons are given why direct coagulation of the tumor by diathermy or similar agents gives far better and more certain lasting results than those reported to be obtained by X rays or radium.

13. The background statistics of this selected group of surgical cases uncannily parallel those found in the general literature of the subject.

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DISCUSSION

DR. EDWIN B. DUNPHY. Very few of us have seen enough cases of angiomatosis retinae to be completely familiar with all aspects of the disease. That is why a thorough survey of the literature, such as has been compiled by Dr. Vail, is so valuable; it brings to our attention the combined experience of many authors.

As far as treatment is concerned, Dr. Vail rightfully emphasizes the many advantages of diathermy and it is comforting to learn that his analysis of 47 eyes treated in this fashion shows that 70 percent were cured.

I should like to report briefly four cases of the disease seen at the Massachusetts Eye and Ear Infirmary.

The first case is that of a forty-eight-year-old male who was admitted to the Massachusetts General Hospital in May, 1932, complaining of headache, dizziness, unsteady gait, and some nausea and vomiting of four months' duration. His general health had always been good and his family history was negative. No localizing signs of brain tumor were found, but fundus examination showed an elevated lesion above the right disc near the periphery with superficial hemorrhages on it and enlarged vessels running into it. There was some detachment of the retina below it. The visual acuity was 20/200 in the right eye and 20/15 in the left. Dr. Verhoeff, who had answered the consultation, pointed out to the neurosurgeons that this was a case of von Hippel's disease and that in all probability there was an accompanying cerebellar cyst. Here is an example of the teamwork which Dr. Vail pleads for in his paper.

A cerebellar exploration was done; the cyst was located and tapped with great relief of the patient's symptoms. Deep X-ray treatment was given to the cerebellum in the hope that it would destroy the cyst. Nothing was done to the eye, since in 1932 ignipuncture was not generally used. The retinal angioma increased in size, with more hemorrhages and exudates and gradual decrease in vision.

There was a return of neurologic symptoms in 1933, 1934, and 1936; great relief was obtained each time by tapping the cerebellar cyst, which was considered inoperable.

The patient died in 1936, and autopsy showed hemangioma of the cerebellum, with cysts in the cerebellum, pancreas, and kidney. The eyes were not obtained.

The second case is that of a sixteen-year-old female, the daughter of the patient just reported. She was first seen in 1939 because of poor vision in the left eye. A diagnosis of typical angiomatosis retinae was made and ignipuncture suggested. This was refused, and she returned six months later with uveitis and secondary glaucoma (Stage IV in Dr. Vail's classification). Enucleation was done. At that time, the right eye was found to be normal.

In October, 1946, she noticed a spot in the nasal field of her remaining right eye. She consulted Dr. Virgil Casten privately, and he found a large angiomatosis in the temporal periphery, fed by enormous vessels. The vision was 20/15. He treated the tumor with flat and perforating diathermy with a successful result. At that time, the neurological exam was negative.

In February, 1957, she was admitted to the Massachusetts General Hospital with a four-year history of numbness in the hands and a three-month history of disturbance in gait. Neurological examination and myelograms indicated a cervical cord tumor. Operation revealed a large cyst opposite C2 and C3, with big vessels coursing through the subarachnoid space. The cyst was drained and she made a good recovery. Her remaining eye had 20/15 vision and looked well except for the chorioretinal scarring from the diathermy operation.

The third case is that of a thirty-seven-year-old female who was first seen in February, 1948. In a routine examination for glasses, a large cyst was found in the lower temporal quadrant of the left eye, which had yellowish exudates on its surface and was fed by large vessels. The vision was 20/25 in the right eye and 20/30 in the left. Neurological exam was negative, although the EEG suggested some disturbance in the posterior half of the left cerebrum.

In May, 1948, diathermy of the cyst was performed by Dr. Alfred Kant, using flat and penetrating electrodes. Considerable reaction followed, with much edema and some hemorrhage which eventually cleared. The retinal tumor shrank in size and vision became 20/25.

The patient was last seen in November, 1956, eight years after operation. Vague neurological symptoms were present, but the eye condition was excellent.

The last case is that of a thirteen-year-old female, first seen in 1949. A gradual loss of vision in the right eye had taken place during the previous year. Family history revealed that the mother had had a blind, painful eye removed, for an unknown cause, in another city ten years previously.

The girl's right eye showed a large tumor below and nasally with hemorrhages and exudates, large feeding vessels, and almost complete detachment of retina. The vision was nil (Stage IV).

The eye was enucleated with pathologic confirmation of clinical diagnosis. The neurologic examination was negative. The left eye was entirely normal with 20/20 vision.

These four cases illustrate several points already brought out by Dr. Vail: (1) familial history; (2) bilaterality; (3) systemic manifestations; and (4) the success of diathermy coagulation if applied early.

It should be stressed that, although the systemic manifestations of this disease may not be obvious at the time the ocular diagnosis is made, they may show up later on. Hence each patient must be under continuing observation, since the earlier the systemic lesions are discovered the better is the chance for saving life.

Most of these retinal tumors and cysts are located near the periphery of the fundus. This is fortunate because it makes them so much more accessible to diathermy treatment.

I agree with Dr. Vail that coagulation by diathermy seems to be the treatment of choice and that the minimum amount of current necessary to do the job should be employed. I would prefer to use first a nonperforating flat electrode to localize the tumor, encircling it with marks that can be identified ophthalmoscopically. After this has been done, a 1.5-mm. perforating electrode can be used in the center of this area, the number of perforations depending on the size of the tumor. The amount of current used is variable but, as Weve suggests, it should be weak and prolonged, such as approximately 30 to 40 Ma. for four to five seconds. No attempt should be made to hit the feeder vessels themselves, for, again quoting Weve, the blood vessels may conduct the heat to other parts of the retina, producing unnecessary damage. The target should be the tumor itself, and, if this is accurately localized, the chances are good for saving the eye from its usual downward course, provided we have recognized the condition early.

DR. F. C. CORDES. As Dr. Vail stated, in 1952, 11 years after radiation, Dr. Schwartz and I reported a case before this Society. However, I agree with Dr. Vail that diathermy is unquestionably the operation of choice, with the possible exception of those cases in which there are multiple lesions in the posterior pole of the eye.

Dr. Vail stated that in his case the lipoidal exudates disappeared over the course of the years. The same thing occurred in our case. It is this phase that

is of particular interest to me. Ophthalmoscopically, we know that the appearance is quite similar, particularly in the early stage, to the exudates that we find in diabetes. Ashton and Duke-Elder feel that those exudates are the result of lipoids leaking out through the defective walls of these aneurysms.

I have here one of Ashton's slides, which Duke-Elder gave to me a few years ago. In it may be seen the association of these lipoidal exudates with the aneurysms. It is true that ophthalmoscopically we see these exudates without any visible aneurysms. However, as Ashton and Friedenwald have shown, in many cases these aneurysms are multiple and are altogether too small to be seen ophthalmoscopically. It may be that when we do not see this exudate in these eyes it comes out of these invisible microaneurysms.

There is another condition, the miliary aneurysms not related to diabetes which occur in young adult males, which many authors feel is a form of angiomatosis retinae. That would seem to confirm this theory. Such cases would seem to suggest that possibly the exudates that occur in angiomatosis retinae may occur either from defects in the vessel walls within the tumor or defects in the vessel walls leading to the tumor. These findings tend to emphasize the importance of early destruction of this lesion if we are going to save the patient's vision.

DR. PHILIP M. LEWIS. I am very glad that Dr. Vail reported this case, because it gives me the opportunity to bring my two cases up to date.

The first one I operated on with the assistance and encouragement of my colleague, Dr. Rychener, in 1941. The second case was done in 1944. The first was reported before the Academy in 1942, and the second was reported before this Society, with the résumé of the first case, in 1947.

The slides which I am about to show you illustrate the appearance of the first eye, done in 1941. As you may have noticed, in Dr. Dunphy's series the eyes that were not operated on were eventually enucleated. This patient does not have much vision; as before the operation, he can count fingers. But he still has his eye.

The next set of slides shows the second case, first seen in 1944. There was a good deal of reaction and hemorrhage in this case, but the vision in the patient's eye is now 20/20 and J1.

I wish to say that I agree most heartily with Dr. Vail's assertion that these tumors should be treated with diathermy. This was my thesis with both cases when I presented them. One was operated on sixteen years ago, the other thirteen years ago.

DR. BRUCE FRALICK. I hate to prolong this discussion, because I think everything has been said. At the same time, however, because it is such a rare entity as far as operative interference is concerned, I feel that we should put on record four eyes operated on at the University of Michigan.

M. B., thirty-four years of age, came in with 20/400 vision in the right eye and a central scotoma. There was a typical angiomatous retinal cyst in the right upper outer quadrant. He was operated on in April, 1941, by the typical diathermy approach which has been described by Dr. Vail. When last seen in June, 1946, we found an atrophic scar in the area of the cyst; the vessels may have been slightly enlarged over the normal vessels, but they were not particularly so, and his vision was 20/30+ in the right eye. A communication of

June, 1957, states that he has had no neurologic disease and his right vision is 20/40, but a central scotoma is present which makes reading difficult.

The second patient was seen by Dr. Falls in 1946, a lady forty-three years of age with a typical retinal angiomatous cyst in her left eye in the inferior temporal quadrant. She had vision of 20/30 and J7, an eye which was worth salvaging. The neurological examination was entirely normal. Dr. Falls did a partially penetrating diathermy operation on this eye without complication; when last seen, in May, 1957, she still had vision of 20/25 and J1, and the cystic angiomatous area was replaced entirely by scar.

The third patient, a lady twenty-two years of age, was first seen by Dr. Falls in February, 1952. She had symmetrical involvement down and out in both eyes. The vision was 20/100 and no reading in the right eye, 20/20 and J1 in the left eye. Soon thereafter he did partially penetrating diathermy coagulation first in one and then in the other eye. When last seen, in July, 1955, the patient had vision of 20/100 in the right eye and 20/20 in the left eye.

Here are four eyes in three patients, all of whom have been operated by the method described by Dr. Vail. In view of our experience with these cases, and further experience with the use of diathermy in retinal separation, we are of the opinion that this is a safe procedure if surface and not penetrating coagulation is used. It offers these people an opportunity to retain a useful eye in spite of an otherwise progressive disease.

DR. HAROLD F. FALLS. Angiomatosis retinae, according to Van der Hoeve, is one of the phakomatoses. These syndromes exhibit hereditary transmission and congenital skin abnormalities (phako-spots) which not infrequently undergo malignant degeneration. Four specific clinical entities are recognized: (1) angiomatosis retinae, (2) neurofibromatosis, (3) tuberose sclerosis, and (4) Sturge-Weber syndrome. All four syndromes manifest dominant inheritance patterns which exhibit incomplete penetrance and marked variance in expressivity. Since each affected individual possesses a different genetic makeup, and also since no one gene acts alone, it is to be anticipated that the gene for angiomatosis retinae will present considerable difference in its clinical expression. This variation in phenotype (clinical expression) is thus quite likely the consequence of the influence of the gene milieu in which the gene for angiomatosis retinae exerts its action.

It is important for the ophthalmologist to be cognizant of the hereditary nature of angiomatosis retinae and to be familiar with its range of protean manifestation. These include calcification in the cerebellum and/or cerebrum, and tumors and cysts in the cerebellum, spinal cord, pancreas, kidney, and other organs. Isolated hypernephroma was the sole manifestation of the syndrome in a female member of a family studied by us, yet her mother and her son both exhibited cerebellar angioma and retinal cystic changes. The ophthalmologist who is acquainted with the vagaries of this syndrome can practice both preventive and corrective medicine, for it is probable, as reported today, that early surgical interference (at least in the eye and cerebellum) can stop the progress of this disease entity.

Affected individuals and the members of their family should be made acquainted with the hereditary nature of the syndrome.

DR. GEORGE N. WISE. The pathology of the late stages of this disease is very similar to that of Coats's disease. As a matter of fact, Coats originally included it as his Group 3. Both are diseases showing obstructed veins microscopically.

We have recently presented evidence to show that in Eales's disease, diabetic retinopathy, retrolental fibroplasia, and venous thrombosis, the fibrovascular proliferation of the inner retinal layers and into the vitreous is not due to the organization of hemorrhage but is a result of inner retinal hypoxia due to venous and capillary obstruction. Under these circumstances, circulatory stagnation beyond the obstruction occurs in the inner retinal layers; Michaelson's vasostimulating factor reappears; and fibrovascular proliferation develops from the regional veins and capillaries.

This same explanation can account for the development of subretinal fibrovascular proliferation in areas of exudative mounds in Coats's disease and the late stages of angiomatosis retinae. Where the mounds of exudate occur, fatty granular cells and lipoid exudate form beneath the retina and mechanically block the choroidal nutrient supply of oxygen to the outer retinal layers. Under such circumstances, with the retinal venous obstruction and circulatory stagnation so prevalent in these diseases, an inner retinal hypoxia develops as before. In the areas of massive exudation, where the choroidal oxygen supply of the outer retina is mechanically blocked, a much greater retinal hypoxia develops in the outer retinal layers. Therefore, in such areas the greatest vasostimulating factor appears in the outer retina. Thus fibrovascular proliferation here tends to be subretinal rather than toward the vitreous.

This would bear out Coats's original prophecy that when these processes were more thoroughly understood the explanation for retinitis proliferans and the subretinal fibrovascular proliferation of his disease might have a common denominator.

DR. RALPH I. LLOYD. I should like to show some fundus paintings of a case under observation since January, 1931. Slide 1 shows the fundus of the blind left eye of a girl of sixteen, who came to the Brooklyn Eye and Ear Hospital clinic, hoping a glass would help. Here is the typical diagnostic feature of angiomatosis retinae: a short circuit allowing arterial blood to pass directly into a vein without the normal reduction in pressure produced by the tremendous increase in cross section area of the capillaries. Since as a result of this condition both artery and vein lose their characteristics, it is necessary to trace the enlarged vessels back to the disc to determine which is artery and which is vein. The lesion is in the ciliary region too far forward to be seen but there is also a quiet lesion above the macula. Probably the first lesion acts as a safety valve, allowing this second lesion to remain without causing trouble. The date of this painting is January 10, 1931. Judging from slides of other cases, I would say the white background is the result of exudate and capillary masses, beneath or in the retina, preventing the chorio-capillaris from contributing the normal red color of the usual fundus picture. This eye later developed cataract, synechia, moderate pain, and increase of intraocular pressure.

Slide 2 shows the right fundus on January 29, 1931. The vision is 20/20 and there is a typical quiet lesion external to the macula with an artery lead-

ing into it and a vein emerging, neither of which is enlarged. Within three months numerous white spots appeared between the lesion and the macula, showing activity which continued.

Slide 3 shows the fundus as it was on November 17, 1931. The lesion is definitely larger and the vessels connected with it are more dilated. The vision is still 20/20, but the white spots are numerous and close to the macula.

Slide 4 shows the fundus on June 29, 1932. The vision is 10/50, there is much more exudate, the macular area is involved, and the vessels and the lesion have increased in size. June 13, 1933, finds the patient with no central vision. The lesion now projects 5 diopters, lifting the retina in the immediate vicinity. This detachment later became very broad. The subsequent history was similar to that of the other eye: cataract, synechia, and glaucoma with moderate pain. In 1936 a Caesarean was done to avoid effects of labor strain, and another was done two years later. Dr. Browder operated for a cerebellar cyst, but found no vessels in the walls. The patient, who was seen recently (June 13, 1957), goes about with a "Seeing Eye" dog, and earns a modest living by typing from dictaphone records. She has complained lately of numbness and muscle weakness in the right arm and leg, suggesting involvement of the arm and leg centers in the cerebrum. We consulted the literature of the period when the patient was first seen, but the use of X rays, then in vogue, was not advised by consultants. The sudden change in three months of a quiescent lesion into an active menace is surprising, but case reports like those we have had here today are the results of progress and were not available in 1931. The number of these cases is small, but close observation and the prompt use of the treatment now available, and so successful, should not be deferred if any sign of activity appears.

DR. DOHRMANN K. PISCHEL. I want briefly to report some interesting findings. It has always interested me that so many cases seemed to remain cured with no relapses. The difficulty probably is that when a relapse occurs the patient does not go back to the original physician, so that the case remains reported as a cure.

A few years ago I was called in consultation by one of my colleagues to see a patient with an early detachment. Fortunately, in this case the berry-like tumor of this disease was still visible. On inquiring into the history, it was found that this patient had been treated by radiation some years previously and had been reported in the literature as a cure. It must therefore be brought out at this time that some cases which have been reported as cured by radiation were only temporary cures. Returning to the case in hand, we operated upon this case and not only were we successful in curing the detachment, but we were able to destroy this small new tumor. This, of course, made me feel that we were pretty successful in having a good cure. But just a few months ago my colleague told me that although everything had remained well until a few months previously, he had then noted a new berry-like tumor in another sector of the fundus. While he was watching it a detachment started to form there, and therefore he was planning to hospitalize the patient in the near future. Summing up, then, I wish merely to point out that this is not always a quiescent disease that can be cured by destroying one tumor. These tumors

may recur, or new tumors may arise. Therefore, the patients must be watched for years after an apparent cure has been achieved.

DR. DERRICK VAIL. I am glad to hear the latest report from the front on Lewis's two cases. They have been in the literature ever since 1941, and I follow with bated breath the progress of these cases. It is nice to know that, after sixteen years in one of his cases and thirteen years in the other, the eyes are in good shape.

Dr. Falls discussed the congenital and hereditary factors in this disease in his usual fluent and most instructive fashion, and we are grateful to him for doing so. My paper actually did not treat much of this, but it is interesting to know that in the literature the surgical cases reported from diathermy followed very closely the typical history of congenital and familial effects.

Dr. Pischel brings out the point that relapses can occur in this condition, and this is mentioned in the body of the paper. I should like to say, however, that it is possible to miss one of these berry-lesions and to think that you are dealing with only one tumor when actually there may be multiple tumors in the far periphery. Statistics show that the majority of the tumors occur in the temporal side, more often in the upper temporal than the lower temporal. They also may occur any place else, of course. A false sense of security may be experienced by destroying the obvious lesion, while the ones that are present in very small size or quantity in the extreme periphery have been missed.

It is also noted in the literature that new berry-like lesions can occur probably almost at any time.

Dr. Wise has given us an excellent discussion on the relationship of the underlying pathological processes that are probably common in a number of conditions of which the most prominent are Coats's disease and angiomatosis retinae in Stages III and IV. I am personally very grateful for this tying-in of a picture that is most confusing, at least to me.

Dr. Lloyd's case shows very well, I think, the progress of the untreated case over a period of two years. As you remember, I said that between Stages I and II a certain interval can elapse which may vary from one to two years, or even longer, before the lipoid degeneration begins. This brings up the point that Dr. Cordes has called to our attention, that is, the method of formation of the lipoid deposit.

I believe that successful surgery will lead to a disappearance of the exudative processes, and this thought is supported by what Dr. Cordes has told you: if the blood vessel walls and the berry-like lesion leaking this lipoid material are destroyed, further leakage does not occur and the lipoid is not laid down; furthermore, the old lipoid is absorbed, although this takes a very long time. Therefore, if after operating on a patient the lipoid is still present at the end of a year or so, it means that the disease is not cured and further search for other berry-like lesions must take place.

I am also very happy that other discussions have reported the additional cases where diathermy coagulation has been used and successfully so.