

prejudice them against a good movement, but should do their part properly to further it.

#### VALUE OF PROPHYLAXIS

The prevention of blindness from this cause is too important to demand argument, too successful to require debate, too necessary to need exaggeration or overstatement. The value of prophylaxis in these cases, one of the greatest triumphs of modern scientific, preventive medicine, has been so clearly proved by carefully computed statistics of incontestable accuracy, often published, secured by responsible medical authorities in many civilized countries, that members of the profession can ill afford to assume an attitude of indifference or presume to question the usefulness of a prophylactic (Gehrung<sup>15</sup>). The solution is easily employed and can be readily secured, is freely distributed by many state health boards, and conscientious physicians should always have fresh, clear solutions in their obstetric bags. The objections to frequent use of prophylactic measures, slight pain and mild silver conjunctivitis in many children who would not be likely to have ophthalmia neonatorum, are not comparable in importance to the almost never-failing success in preventing this no longer necessarily venereal or shame disease. The great lying-in hospitals in which cases of ophthalmia neonatorum and its results were formerly so conspicuous, very rarely have any such cases since the routine use of some good method of prophylaxis. That some physicians of large experience have not had any cases of severe ophthalmia neonatorum is their good fortune, but only begets a false sense of security for the future. It is not a parallel argument to say that because some people die of appendicitis, therefore, every appendix should be removed. Such a course would be attended with risks out of proportion to the results to be obtained. The prophylactic properly used is practically never dangerous. It is not true that a drop placed in the eye after inflammation has once begun is the same as one used soon after birth. In the latter case, unless inflammation is already established, there are probably only a few germs along the margins of the lids; in the former they are distributed throughout the conjunctival sac in its folds and recesses and will therefore require severe treatment to destroy them. It is difficult to understand the indifference of many physicians to this important subject, about which so much is being written, for many such physicians are men who frankly condemn and recommend prosecution of quacks, Christian Scientists, etc., for their malpractice and vagaries. The time is nearly here when the accoucheur and nurse will be subjected to severe criticism and reproach, whether deserved or not, and considered culpably negligent and censurable in every case in which ophthalmia neonatorum develops, especially if measures for its prevention have been neglected, as nurse and physician are now blamed if proper aseptic precautions for the protection of the mother against infection are not observed.

165 East Market Street.

[THE DISCUSSION ON THIS PAPER WILL BE FOUND ON A LATER PAGE OF THIS ISSUE UNDER THE HEADING OF "SECTION DISCUSSIONS."]

**Criminals and Defectives.**—When a criminal is referred to as "defective," a misconception is liable to be created, as the general impression made by the word is that of physical deformity. Yet, he is strictly speaking within the meaning of the word, for he is incompetent.—*Jour. Crim. Law and Criminology.*

15. Gehrung: *New York State Jour. Med.*, ix, No. 5, p. 205.

## THE SIGNIFICANCE OF RETINAL HEMORRHAGE

BASED ON A STUDY OF THE SUBSEQUENT HISTORY OF ONE HUNDRED AND EIGHTY-SEVEN CASES \*

F. T. ROGERS, M.D.

PROVIDENCE, R. I.

The various types of retinitis seen during a practice of more than a score of years have emphasized the fact that the therapeutic measures at our command in this condition are practically valueless. If recovery occurs, it must be ascribed to the recuperative powers of Nature, rather than to any effort of our own. Except in the albuminuric type, the prognostic significance of the disease has not been sufficiently appreciated to warrant the text-books in succinctly stating the fact, or to influence us in caring for the future welfare of the patient rather than devoting our entire energies to the relief of the existing condition.

It was to ascertain whether other than the albuminuric forms of retinitis were as significant of grave termination that I have made a study of 187 cases of retinitis occurring in private practice since 1890. The much larger number seen in my hospital service has been omitted because of my inability to trace the subsequent history of the patients. Specific retinitis has been omitted because of its nature, and because of the fact that it is usually much more amenable to treatment than the non-syphilitic types.

It has been my practice to diagnose my cases under one of six heads:

1. Retinal apoplexy, due to,
  - (a) A rupture of the walls of a vessel;
  - (b) Diapedesis.
2. Simple retinitis, secondary to retinal apoplexy.
3. Hemorrhagic retinitis with secondary hemorrhages.
4. Albuminuric retinitis.
5. Diabetic retinitis.
6. Chorioretinitis.

While the classification may be deemed imperfect, it serves to eliminate the forms of retinitis which are not associated with hemorrhages and affords the information desired for the present inquiry.

Text-books on ophthalmology, with few exceptions, pass the subject of prognosis with the statement that "retinal apoplexy and hemorrhagic retinitis are of grave import," "a forerunner of cerebral apoplexy," or "an indication of grave vascular or cardiac lesions," while they are united in the opinion that albuminuric retinitis is fatal within a short time in 70 per cent. of cases. This part of the subject has been ably discussed by various authors, and the statistics of the cases of albuminuric retinitis are offered merely as corroborative evidence of the gravity of the condition, yet the statement of Porter that "all cases of albuminuric retinitis are found in syphilitics," is so abundantly disproved by my own cases that I cannot forbear to call attention to them. The comparatively few diseases which are ascribed as the cause of death in my fatal cases emphasize our present knowledge of the etiology of hemorrhagic retinitis, which may be briefly summed up as follows:

1. Atheroma.
2. Vasculitis and perivasculitis.
3. Increased arterial or venous pressure.

\* Read in the Section on Ophthalmology of the American Medical Association, at the Sixty-Second Annual Session, held at Los Angeles, June, 1911.

4. Altered condition of the blood found in nephritis, glycosuria, oxaluria or profound toxemia.
5. Traumatism.
6. Reflex disturbances.

All the deaths which have occurred may be ascribed to one of these six causes.

I have records of 240 cases of retinitis, and of these I have been able to trace the subsequent histories of 187. I am unable to account for fifty-three. Seventy-four are living and 113 are dead.

TABLE 1.—SHOWING OUTCOME IN 187 CASES OF VARIOUS TYPES OF RETINITIS

Type of Disease	No. of Patients	Living	Dead	Per cent. Dead
Retinal apoplexy	22	17	5	22.7
Hem. retinitis	47	21	26	55.3
Alb. retinitis	101	23	78	74.2
Diab. retinitis	10	5	5	50.0
Chorioretinitis	7	5	2	28.6
	187	74	113	60.4

So far as may be judged by such a small number of cases, 60 per cent. of all cases of non-syphilitic hemorrhagic retinitis terminate fatally within a few years; while of the hemorrhagic type a much larger number (55.3 per cent.) than is generally believed, are rapidly fatal. Any disease in which more than half of the

TABLE 2.—STATE OF HEALTH OF LIVING PATIENTS

	Period of Observation						Diseases								Total	
	One Year.	Two Years.	Three Years.	Five to Ten Years.	Over Ten Years.	Total.	Usual Health.	Poor Health.	Blind.	Hemiplegia.	Paralysis Agitans.	Epilepsy.	Mental Disease.	Arterio-sclerosis.		Rheumatism.
Ret. apoplexy	6	4	..	1	6	17	10	..	1	4	..	..	..	..	2	..
Hem. retinitis	3	5	1	12	..	21	11	1	3	..	1	2	2	1	..	..
Alb. retinitis	7	9	2	6	2	20	14	9	3	..	..	..	..	..	..	..
Diab. retinitis	2	..	1	..	2	5	..	3	1	1	..	..	..	..	..	..
Chorioretinitis	..	2	..	1	2	5	5	..	..	..	..	..	..	..	..	..
	18	20	4	20	12	74	40	13	8	5	1	2	2	1	2	74

patients die within a short time is worthy of careful study.

We may gain valuable information by a consideration of the state of health of those now living, and in all cases of which I have not personal knowledge I have gained my information from the family physician.

Of the seventy-four living patients thirty-four, or 46 per cent., are in confessedly poor health, and the similarity between the specific diseases from which they suffer and the causes of death shown in Table 3 warrants the assumption that the mortality there shown will in a short time be increased.

I desire also to call attention to the fact that it is hemorrhagic retinitis which yields the larger percentage of the cases of poor health.

TABLE 3.—CAUSES OF DEATH

	Nephritis.	Cerebral Tumor.	Apoplexy.	Diabetes.	Arterio-sclerosis.	Pulmonary Tuberculosis	Suicide.	General Paresis.	Cardiac Disease.	Rheumatism.	Diphtheria.
Ret. apoplexy	..	..	3	..	..	..	..	..	1	..	5
Hem. retinitis	..	5	12	..	1	..	2	..	2	..	26
Alb. retinitis	75	..	..	..	..	..	..	..	..	..	75
Diab. retinitis	..	..	..	4	..	..	..	..	..	1	5
Chorioretinitis	..	..	2	..	..	..	..	..	..	..	2
	75	5	17	4	2	2	2	1	3	1	113

TABLE 4.—DURATION OF LIFE

Causes of Death	Died within 6 months.	Died 6 mos. to 1 year.	Died 1 to 2 years.	Died 3 to 10 years.	Died over 10 years.	Total.
Nephritis	38	15	10	10	2	75
Cerebral tumor	1	2	1	1	..	5
Apoplexy	..	7	1	7	..	17
Diabetes	13	..	2	..	..	15
Arteriosclerosis	..	..	..	12	..	12
Pulmonary tuberculosis	1	..	..	1	..	2
Suicide	..	1	..	1	..	2
General paresis	..	..	1	..	..	1
Cardiac disease	..	..	1	2	..	3
Rheumatism	..	..	1	1	..	2
Diphtheria	..	..	1	..	..	1
	44	25	17	25	2	113

TABLE 5.—AGES OF FATAL CASES OF NEPHRITIS

Age Group	No. of Cases	Average Duration of Life
Under twenty years	1	2 weeks
Twenty to thirty years	12	5 months
Thirty to forty years	11	8 months
Forty to fifty years	9	30 months
Fifty to sixty years	25	18 months
Sixty to seventy years	13	20 months
Seventy to eighty years	4	27 months
Over eighty years	1	2 months
	75	

TABLE 6.—DURATION OF LIFE IN FATAL CASES OF NEPHRITIS

One day, 1 case; 2 days, 1 case; 1 week, 1 case; 2 weeks, 3 cases; 1 month, 6 cases; total, 12, or 15 per cent., died within one month.  
 Two months, 5 cases; 3 months, 10 cases; 4 months, 7 cases; 5 months, 2 cases; 6 months, 3 cases; total, 30, or 52 per cent., died within six months.  
 Seven months, 1 case; 9 months, 3 cases; 10 months, 1 case; 11 months, 3 cases; 1 year, 7 cases; total, 54, or 72 per cent., died within one year.  
 Eighteen months, 2 cases; 19 months, 1 case; 20 months, 1 case; 24 months, 6 cases; total, 64, or 85 per cent., died within two years.  
 Three years, 5 cases; total, 69, or 92 per cent., died within three years.  
 Five years, 1 case; 6 years, 1 case; 8 years, 2 cases; 10 years, 1 case; 12 years, 1 case; total, 75.

TABLE 7.—DURATION OF LIFE IN ALL CASES

	Cases	Per Cent.
Living at end of ten years or more	74	40.9
Died in one year	70	37.4
Died in two years	17	9.0
Died in three years	4	2.1
Died in three to ten years	19	10.1
Died after ten years	3	0.5
	187	100.0

Chances of death in 1 year, 37.4 per cent.  
 Chances of death in 2 years, 46.4 per cent.  
 Chances of death in 3 years, 48.5 per cent.

If these statistics are correct (and I have taken great pains in their preparation, in which I have been greatly assisted by my associate, Dr. J. W. Leech), a study of their findings will reveal what I have endeavored to prove, i. e., that aside from the well-known, speedily fatal termination of albuminuric retinitis, not only simple

retinal apoplexy, but all the types of retinitis associated with hemorrhages are danger signals, and that our duty lies more in the safeguarding of the patient's future than in the treatment of the present ailment. It offers to life insurance examiners the possibility of forecasting the future of an applicant, and thus determining his value as a risk with more accuracy than by the ordinary methods of examination, and suggests the advisability of insisting on an ophthalmoscopic examination in every case. The comparatively small number of cases, of course, weakens our conclusions, but what is true of the whole is in a measure true of its parts, and further investigations by other observers will, I believe, corroborate these findings. Of the 187 patients 113 (60 per cent.) are dead and thirty-four are in poor health, and only forty (21.4 per cent.) are reported as in their usual health. Of those who suffered from retinal apoplexy 45 per cent. are in good health, while in the cases of hemorrhagic retinitis but 24 per cent. of the patients are not either dead or afflicted with some grave disorder. Thirteen per cent. only of the patients with albuminuric retinitis are alive and well, and of the diabetic type there is none.

#### CONCLUSIONS

1. Three-quarters of all cases of hemorrhagic retinitis either terminate fatally within a few years or the patients suffer marked impairment of health.

One patient died of diphtheria during an epidemic, but was suffering from Bright's disease, and her life would in any event have been of short duration. One died of rheumatism, four from diabetes, and of the two who died of tuberculosis, one certainly did not have that disease when seen, but she died suddenly while returning from Europe and the cause of death was given as tuberculosis.

With these exceptions, all deaths have been due to some disorder of the nervous or circulatory system, and all cases of impaired health are ascribed to the same conditions.

2. The existence of any form of hemorrhagic retinitis is suggestive of present or future disease of either the nervous or circulatory system.

By reference to Table 5, it will be noticed that the average duration of life in albuminuric retinitis increases regularly with the age of the patients. An apparent exception is found between the ages of forty and fifty, but this is due to the fact that the two patients who lived ten and twelve years, respectively, were between these ages. If these are eliminated, the average duration is twelve months. The largest number of cases occur between the ages of forty and fifty.

3. The duration of life in albuminuric retinitis increases with the age of the patient and the younger the patient, the worse the prognosis in point of time.

There have been nine cases of albuminuric retinitis occurring in pregnancy, and of these, two of the patients are dead of acute uremia; one two weeks after parturition at term, the other at four months. Of the seven patients living all are in excellent health; three have passed subsequent pregnancies without recurrence, five have vision of 0.9, or better, and in two there is impaired vision.

When, in the etiology of any disease, reflex disturbance is given as a cause, it is usually synonymous with lack of accurate knowledge. My warrant for ascribing hemorrhagic retinitis to such a cause is found in two cases which I desire to report in detail.

CASE 1. E. G., aged 36, a bank clerk, was first seen in 1898 with a myopia of one diopter, which, when corrected, gave him normal vision in each eye. January 28, 1903, he was again seen, and with the correcting glass his vision was 1.0 in each eye. February 2, while at the dentist's a drill perforated the root of a first bicuspid tooth on the right side of his jaw, and breaking, a portion was left in the tooth. Almost immediately there was a blurring of vision in the right eye, and on the following morning when I saw him there was an extensive retinal hemorrhage just above the macula, the vision being reduced to 2/50. The tooth was extracted and the broken tip of the drill was found protruding about  $\frac{1}{4}$  of an inch. The splash of hemorrhage was soon surrounded by an area of edema, and several spots of exudation appeared in the macular region, which rapidly increased till they presented the appearance of finger-like projections extending into the vitreous, which waved back and forth with the motion of the globe. In June, of that year, this exudate had disappeared, leaving dirty yellow spots, but the vision was not improved. I did not see him again until June, 1906, when to my surprise the vision was again normal. The retina had resumed its normal appearance, save that one of the ascending arteries was obliterated for about two diameters, and a collateral circulation had been established.

This patient was seen in consultation by Dr. Hasket Derby, of Boston, and he expressed his opinion that the retinitis was a reflex disturbance.

A pertinent fact in connection with this case was that an indemnity on an accident insurance policy was denied on the ground that it was not accidental.

CASE 2. In 1905, I saw Miss E. J., aged 40, who noticed on the day following a visit to the dentist that the vision of one eye was blurred. She had been having a nerve killed and had suffered a good deal of pain at the time, but did not ascribe her loss of vision to anything connected with her tooth. She presented numerous splashes of hemorrhage in the retina of the right eye, and with the memory of the first case in my mind, I spoke of the possibility of a similar condition. She immediately consulted her dentist, who assured her that there was no possibility of such an accident, but on the third day she insisted on having the tooth extracted, and, with the dentist, visited my office, bringing the offending molar. It showed no evidence of having been injured, but to make assurance more sure, I made a section of the tooth in the axis of the dental canal and found in it a broken piece of steel broach, a quarter of an inch long. The retinitis resulting subsided in about three months, leaving normal vision.

These two cases can hardly be ascribed to a coincidence.

The following case illustrates the point I desire to make.

CASE 3. A. B., aged 40, unmarried, was referred to me on account of severe headaches. There was no history of specific infection, the previous condition of health was excellent, and his physician, failing to find an adequate cause for the headaches, as usual ascribed it to the eyes. He had several spots of retinal hemorrhage evidently of recent occurrence, but no impairment of vision. He was referred to his home physician for a urinalysis and I did not again see him for several weeks, when he reappeared with greatly diminished vision and an active neuroretinitis of each eye. He said that no trouble had been found with his urine and that his physician had, in the absence of other symptoms, given him potassium iodid in 5-grain doses, which he had been taking since I first saw him. Evidently cerebral disturbance was present, and a letter was given him to deliver to his physician, stating my opinion that the trouble was due to a cerebral tumor and that the prognosis was bad. He died on the way home while on the train and the letter was taken from his pocket by the medical examiner called to the case.

If there had been an appreciation of the gravity of this case and more attention given to its possibilities, the fatal termination possibly could have been delayed.

I have endeavored to show by these statistics that all types of hemorrhagic retinitis are of serious import; that even retinal apoplexy is significant of impending danger, while simple retinitis with hemorrhage has a mortality largely in excess of that commonly ascribed to it. I have made no study of the pathology, and make no suggestion for treatment, except to urge that attention be given to the future of the patient and not to the present.

117 Broad Street.

[THE DISCUSSION ON THIS PAPER WILL BE FOUND ON A LATER PAGE OF THIS ISSUE UNDER THE HEADING OF "SECTION DISCUSSIONS."]

## CULTIVATION OF PATHOGENIC TREPONEMA PALLIDUM \*

HIDEYO NOGUCHI, M.D.  
NEW YORK

Although several investigators (Scherschewsky, Mühlens and Hoffmann) have secured cultures of certain spirochetes, no one has yet been able to establish them as being undoubted examples of *Treponema pallidum* (*Spirochata pallida*). In some instances, the morphologic features of the organisms in the cultures were identical with those present in syphilitic lesions in man, yet they never caused lesions when inoculated into animals. In two exceptional instances, Bruckner and Galasesco, in 1910, and Sowade, in 1911, reported that they had succeeded in reproducing syphilitic lesions in the rabbit by the injection of "impure cultures." But as these "cultures" still contained the original syphilitic tissue used for inoculation, and as a second growth (generation) of the spirochetes could not be obtained, it remained an open question whether the lesions were due actually to the cultivated spirochetes or whether they were simply produced by the original spirochetes that had survived.

### METHOD OF CULTIVATION

All previous investigators used human syphilitic tissues for the cultivations. I have employed only the spirochete-containing testicular tissue of the rabbit. As is well known, this tissue, at the height of the lesions, contains innumerable motile spirochetes. The rabbit material is available at all times and tends, when continuous passages have been effected, to contain relatively few common bacteria. Up to the present time, I have employed ten different strains of *Spirochata pallida*, all of which have been passed through the rabbit. Of these, six strains have been passed through successive series of cultures.

The only suitable culture-medium which I have thus far found is serum-water (sheep, horse, rabbit) to which a piece of sterile rabbit tissue is added. I have preferred the kidney or testicle. The liver is less suitable, first, because it often contains bacteria, and, second, because of the large quantity of carbohydrate which in the presence of the common bacteria yields a large amount of acid. Test-tubes 20 cm. high and 1.5 cm. wide are chosen into which 16 c.c. of the serum-water are introduced. After sterilization at 100 C. for three successive days, a small piece of the freshly removed organ is added. The tubes, having been incubated at 37 C. for two days, are, if sterile, ready for use. A layer of paraffin oil is poured into each tube to shield the medium from the air and to prevent evaporation. In

order to obtain the first growths of the spirochetes, no agar or gelatin should be added to the medium; later generations can, however, be secured in a solid medium. At first, strict anaerobiosis is required, but later this strictness is not essential. Indeed, certain strains of *Spirochata pallida* grow in later generations in a deep serum agar culture in which the tissue is placed at the bottom which is merely covered with paraffin oil. In no case did any of the strains grow in the absence of tissue. In this respect they differ greatly from those described by Mühlens and Hoffmann, which grew readily not only in the absence of tissue but even of serum.

In almost all the first growths, the spirochetes are mingled with bacteria. As the *Spirochata pallida* do not grow at this time in solid media, purification is difficult. I have obtained this by permitting the spirochetes to grow through Berkefeld filters that hold back the ordinary bacteria for a longer period. This is accomplished after about the fifth day. Or the strains which, after a time, begin to grow in solid media may be separated from the bacteria by reason of the fact that while the latter remain confined to the stab-canal, the former penetrate, as a slight haze, into the surrounding medium, from which they can be removed in a pure state. Thus cultivated, the morphology is correct for the *Spirochata pallida*, and motility is retained for some weeks. As would be expected from the conditions of growth, special arrangements and groupings of the spirochetes occur in the cultures.

### PATHOGENICITY

Two strains of the *Spirochata pallida* in pure culture have thus far been tested for pathogenicity by inoculation into the testicle of rabbits, and both have set up the typical lesions. The first strain was cultivated in October, 1910, the second in March, 1911. The aspirated fluid, taken during life, showed innumerable spirochetes which, viewed under the dark-field microscope or after Giemsa staining, presented the characteristic qualities of *Treponema pallidum*. The testicular tissue, stained with the usual histologic dyes or impregnated with silver salts by Levaditi's method, showed the usual cellular infiltration and countless spirochetes, precisely as after successful inoculation with syphilitic material from human beings.

### CONCLUSION

It may be affirmed that *Treponema pallidum* has been made to grow in pure culture and that the cultures possess the usual pathogenicity for the rabbit.

It may be further stated that the testicular lesions produced in the rabbit by means of pure cultures of the *Spirochata pallida* are identical with those set up by syphilitic materials, from which it follows that the cause of the syphilitic lesions in man, as of the testicular lesions in the rabbit, is *Treponema pallidum*.

The method will be described in detail in a forthcoming number of the *Journal of Experimental Medicine*.

**So-Called Thyroid Carcinoma of Brook Trout.**—There is no stage of thyroid hyperplasia in brook trout that may be classified biologically as carcinoma. The incidence of true carcinoma in fish goiter is not greater than in mammalian goiter. Goiter is endemic in all hatcheries where the *salmonidae* are artificially reared. Its severity is quantitatively related to the general hygienic conditions prevailing, and to the food, water-supply and degree of crowding. The immediate cause of goiter is unknown, but it depends in all probability on a disproportion in, or a lack of, certain of the elements necessary for proper nutrition.—D. Marine and C. H. Lenhart, in *Journal of Experimental Medicine*.

\* From the Laboratories of the Rockefeller Institute for Medical Research.