



*Bulletin* of the

**University of Minnesota Hospitals  
and  
Minnesota Medical Foundation**



**Papilledema, Papillitis,  
Pseudo-neuritis**

BULLETIN OF THE  
UNIVERSITY OF MINNESOTA HOSPITALS  
and  
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I. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL  
CALENDAR OF EVENTS

April 3 - 9, 1949

No. 242

Sunday, April 3

- 9:00 - 10:30 Surgery Grand Rounds; Station 22, U. H.  
10:30 - 11:00 Factors in the Production of Intestinal Gases; Fred Cross; Rm. M-109,  
U. H.

Monday, April 4

- 8:00 - Fracture Rounds; A. A. Zierold and Staff; Ward A, Minneapolis General  
Hospital.  
9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and  
Staff; Todd Amphitheater, U. H.  
9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff;  
M-109, U. H.  
10:00 - 12:00 Neurology Rounds; A. B. Baker and Staff; Station 50, U. H.  
11:00 - 11:50 Physical Medicine Seminar; Hypoxia Fever Therapy; William Kubicek;  
E-101, U. H.  
11:00 - 11:50 Roentgenology-Medicine Conference; Veterans Hospital.  
11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Eustis Amphitheater, U. H.  
12:00 - 1:00 Physiology Seminar; The Delay of Senescence in Fertility by Dietary  
Restriction; Mrs. Claire J. Carr; 214 M. H.  
12:15 - 1:20 Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H.  
12:30 - 1:20 Pathology Seminar; Carcinoma of the Lung in Veterans; B. J. O'Laughlin,  
104 I. A.  
12:30 - 1:30 Surgery Problem Case Conference; A. A. Zierold, C. Dennis and Staff;  
Small Class Room, Minneapolis General Hospital.  
1:30 - 2:30 Surgery Grand Rounds; A. A. Zierold, C. Dennis and Staff; Minneapolis  
General Hospital.  
1:30 - 2:30 Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H.  
4:00 - Pediatric Seminar; Secondary Shock; W. LeBien; 6th Floor, Child  
Psychiatry, U. H.  
5:00 - 5:50 Clinical Medical Pathologic Conference; Todd Amphitheater, U. H.

5:00 - 6:00 Urology-Roentgenology Conference; D. Creevy and H. M. Stauffer and Staffs; M-109, U. H.

Tuesday, April 5

- 8:00 - 9:00 Fracture Conference; Auditorium; Ancker Hospital.
- 8:30 - 10:20 Surgery Seminar; Carcinoma of the Pancreas and Ampullary Region; C. W. Howell; Small Conference Room, Bldg. I, Veterans Hospital.
- 9:00 - 9:50 Roentgenology Pediatric Conference; L. G. Rigler, I. McQuarrie and Staff; Todd Amphitheater, U. H.
- 10:30 - 11:50 Surgical Pathological Conference; Lyle Hay and Robert Hebbel; Veterans Hospital.
- 12:30 - Pediatric-Surgery Rounds; Sta. I, Minneapolis General Hospital; Drs. Bosma, Wyatt, Chisholm, McNelson and Dennis.
- 12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.
- 1:00 - 2:30 X-ray Surgery Conference; Auditorium, Ancker Hospital.
- 2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III, Veterans Hospital.
- 3:15 - 4:20 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U. H.
- 3:30 - 4:20 Clinical Pathological Conference; Staff; Veterans Hospital.
- 4:00 - 5:00 Pediatric Rounds on Wards; I. McQuarrie and Staff; U. H.
- 4:00 - 5:30 Physiology-Surgery Conference; Neurogenic Pulmonary Edema; Drs. G. Campbell, F. Haddy, S. Zinberg, L. French; Eustis Amph., U. H.
- 5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Todd Amphitheater, U. H.
- 5:00 - 6:00 X-ray Conference; Dr. Lipschultz and Staff; General Hospital; Todd Amphitheater, U. H.

Wednesday, April 6

- 8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-515, U. H.
- 8:30 - 9:30 Clinico-Pathological Conference; Auditorium, Ancker Hospital.
- 8:30 - 10:00 Orthopedic-Roentgenologic Conference; Edward T. Evans; Room 1AW, Veterans Hospital.
- 8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker and Joe R. Brown; Veterans Hospital.
- 11:00 - 12:00 Pathology-Medicine-Surgery Conference; O. H. Wangensteen, C. J. Watson and Staff; Todd Amphitheater, U. H.

- 12:00 - 12:50 Radio-Isotope Seminar; Determination of Tissue Dosage by Radio-Active Isotopes; J. C. Wang; Rm. 212, Hospital Court, Temp. Bldg.
- 3:30 - 4:30 Journal Club; Surgery Office, Ancker Hospital.
- 4:00 - 5:00 Infectious Disease Rounds; Main Lecture Room, Minneapolis General Hospital.

Thursday, April 7

- 8:15 - 9:00 Roentgenology-Surgical-Pathology Conference; Craig Freeman and H. M. Stauffer; M-109, U. H.
- 8:30 - 10:20 Surgery Grand Rounds; Lyle Hay and Staff; Veterans Hospital.
- 9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; M-109, U. H.
- 10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.
- 10:30 - 11:50 Surgery-Radiology Conference; Daniel Fink and Lyle Hay; Veterans Hospital.
- 11:00 - 12:00 Cancer Clinic; K. Stenstrom and A. Kremen; Todd Amphitheater, U. H.
- 11:30 - 12:30 Clinical Pathology Conference; Steven Barron, C. Dennis, George Fahr, A. V. Stoesser and Staffs; Large Class Room, Minneapolis General Hospital.
- 12:00 - 1:00 Physiological Chemistry Seminar; 214 M. H.
- 1:00 - 1:50 Fracture Conference; A. A. Zierold and Staff; Minneapolis General Hospital.
- 2:00 - 3:00 Errors Conference; A. A. Zierold, C. Dennis and Staff; Large Class Room, Minneapolis General Hospital.
- 4:00 - 5:00 Bacteriology and Immunology Seminar; Enzyme Systems of Viruses; Ralph Wands; 214 M. H.
- 4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hansen and Staff; E-534, U. H.
- 5:00 - 6:00 Urology Seminar; Ureterolithotomy; Brian McGroarty; E-101, U. H.
- 5:00 - 6:00 X-ray Seminar; Case Reports, Miller Hospital; Drs. Peterson and Miller; Todd Amphitheater, U. H.

Friday, April 8

- 8:30 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.
- 9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.
- 10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.
- 10:30 - 11:20 Medicine Grand Rounds; Staff; Veterans Hospital.

- 10:30 - 11:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.
- 11:00 - 12:00 Surgery-Pediatric Conference; C. Dennis, O. S. Wyatt, A. V. Stoesser and Staffs; Minneapolis General Hospital.
- 11:30 - 12:50 University of Minnesota Hospitals General Staff Meeting; Control of Human Epiphyseal Growth; Douglas T. Lindsay; Powell Hall Amphitheater.
- 12:00 - 1:00 Surgery Clinical Pathological Conference; Clarence Dennis and Staff; Large Classroom, Minneapolis General Hospital.
- 1:00 - 1:50 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.
- 1:00 - 3:00 Pathology-Surgery Conference; Auditorium, Ancker Hospital.
- 1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.
- 4:00 - 5:00 Electrocardiographic Conference; George N. Aagaard; 106 Temp. Bldg., Hospital Court, U. H.

Saturday, April 9

- 7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 20, U. H.
- 8:30 - 9:30 Surgery Conference; Auditorium, Ancker Hospital.
- 8:00 - 9:00 Pediatric Psychiatric Rounds; Reynold Jensen; 6th Floor, West Wing, U. H.
- 8:00 - 9:00 Surgery Literature Conference; Clarence Dennis and Staff; Minneapolis General Hospital, Small Classroom.
- 9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; E-101, U. H.
- 9:00 - 10:30 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater, U. H.
- 9:00 - 11:30 Surgery-Roentgenology Conference; Todd Amphitheater, U. H.
- 9:00 - 12:00 Psychiatry Conference; VA Hospital Annex, Fort Snelling.
- 10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.
- 10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.
- 11:00 - 12:00 Anatomy Seminar; Hepatic Studies with Rose Bengal, W. L. Williams; Mitochondria in Cell Bodies of the Hypoglossal Nucleus and of Spinal Ganglia Following Section of Nerves, J. F. Hartman; 226 I. A.

## II. PAPPILLEDEMA, PAPPILLITIS, PSEUDO-NEURITIS

Llewellyn E. Christensen

### Introduction

The recognition and differentiation of these three clinical entities are, as we know, frequently very difficult. In fact, in some few cases a differentiation may well be impossible for a given observation period. The importance of early differentiation is, of course, in the type of treatment to be instituted and prognosis attached. It has seemed appropriate, therefore, to review the literature on these subjects in an attempt to bring out the salient ophthalmological features which may help us all in recognizing and differentiating these conditions.

### History and Definitions

The early ophthalmoscopists described all cases in which there were acquired changes in the optic discs other than pallor and atrophy as "optic neuritis" 1,2,3. When the swelling of the nerve head was great, it was called "choked disc".<sup>3</sup> Somewhat later the observers recognized that in some of these cases there was marked loss of vision and in others there was no change or only slight decrease in visual acuity. It was therefore apparent that this so-called "optic neuritis" must have more than one origin. By 1911 there was a clear-cut differentiation regarding the etiology of swelling of the optic discs.<sup>4</sup>

The term, papilledema, was first used to describe passive edema of the discs due only to increased intra-cranial pressure.<sup>3</sup> It is now properly used to describe passive non-inflammatory edema of the discs from any cause.<sup>4</sup> The most important cause is still increased intra-cranial pressure; however, other causes may be blood dyscrasias, orbital tumor, focus of optic nerve inflammation just proximal to the nerve head, and others to be mentioned later. "Choked disc" is a term which is now taken to signify that

papilledema has occurred because of increased intra-cranial pressure from brain tumor or tumor equivalent (brain abscess, cysts, venous sinus thrombosis, etc.)<sup>4</sup>

The term, optic neuritis, is now used to describe inflammatory or demyelinating conditions of the optic nerve. The condition then may be designated according to the site of involvement as follows:<sup>4</sup>

- (1) intra-ocular optic neuritis
- (2) intra-ocular optic neuroretinitis
- (3) papillitis (synonymous with intra-ocular optic neuritis but confined to the nerve head)
- (4) retro-bulbar optic neuritis
- (5) optic perineuritis (inflammation of optic nerve sheaths)

Lastly, the observers were confronted with certain congenital anomalies of the optic disc which had to be differentiated from papilledema primarily, but also from optic neuritis. Medullated nerve fibers at the disc, persistent hyaloid tissue, and fibrous tissue on the disc were quite readily recognized as such. However, the congenital condition in which the nerve fibers with an excess of glial tissue are heaped up on the disc to form an elevation did present a definite differential diagnostic problem.<sup>5</sup> Such a condition is referred to as pseudo-neuritis or spurious optic neuritis.

### Etiology, Pathogenesis, Pathology

#### 1. Papilledema

In general terms, the cause of papilledema may be described as a disturbance of the normal pressure relationship of the circulation (of blood and either tissue fluid or cerebro-spinal fluid) on either side of the lamina cribrosa.<sup>5</sup> Such a disturbance may result from several causes.<sup>5,6</sup>

##### a. intra-cranial

A rise in intra-cranial pressure accounts for a great majority of

the cases of papilledema. This rise may be due either to:

- (1) an increase in cerebral contents (i.e., neoplasm - alone responsible for 71% of the cases of bilateral papilledema - inflammatory growths, blood-clots, increase in volume of cerebro-spinal fluid as in meningitis, or general edema of the brain in systemic disease as anemia or nephritis) or,
- (2) a lack of normal cranial capacity (e.g., oxycephaly).

#### b. orbital

An orbital mass pressing on the optic nerve so that the circulation is impeded is an important cause of unilateral papilledema. This has been brought about experimentally in animals by ligating or clamping the nerve. When the ligature was placed on the nerve proximal to the entrance of the central vessels, the effect was less than when placed distal to the entrance of the vessels. The papilledema was found to be greatest when the central vein and not the artery was included in the ligature.<sup>5</sup>

#### c. ocular

Papilledema due to decreased ocular tension has been observed clinically and numerous cases have been reported.<sup>7,8</sup> This has been produced experimentally in rabbits, dogs, and monkeys by reducing the intra-ocular pressure by trephining.<sup>9</sup>

#### d. general diseases

Papilledema with some general diseases is explained by the definite cerebral edema and increased intra-cranial pressure associated with them.<sup>4,5</sup> These diseases include anemias, nephritis, hypertension, and the toxic states.

Although the exact mechanism of the formation of papilledema is still unknown, the consensus favors the aforementioned

mechanical explanation of circulatory obstruction in the region of the optic nerve. The facts of the occurrence of papilledema with a low intra-ocular or a high intra-cranial pressure, and its dramatic disappearance with a change of the pressure to a normal level are incompatible with any of the non-mechanical theories (inflammatory and vaso-motor).<sup>5</sup> Opinions differ, however, as to what the precise mechanism is for this obstruction. Most of these opinions are based first on the demonstration that the inter-vaginal space of the nerve is in free anatomical communication with the sub-arachnoid space of the brain and that a fluid-pressure can readily be transmitted from one to the other. The theories may be divided into four groups:<sup>4,5</sup>

##### a. venous obstruction in the region of the optic nerve

This localized obstruction has been placed at the cavernous sinus, at the nerve-head itself, and in the inter-vaginal space. Compression of the vein in the inter-vaginal space has received the strongest support because of the many pathological studies of papilledema cases which showed distension of the inter-vaginal space, distension of the central vein in the distal part of the nerve, and marked compression of the central vein in the inter-vaginal space.<sup>10,11</sup> It has also been demonstrated that there is a fairly close relationship between the venous pressure at the disc and the intra-cranial pressure. In order to maintain circulation the venous pressure stays 2-4 mm. Hg. above the intra-cranial pressure and rises to maintain this difference as the intra-cranial pressure increases. When the intra-cranial pressure reaches the intra-ocular arterial pressure, the circulation will cease. It was also shown that when the normal relationship of the pressures in the central vein and artery<sup>(1-3)</sup> is markedly disturbed, papilledema develops. If the arterial pressure increased with the



venous and intra-cranial pressures, edema did not occur.<sup>5</sup>

Such venous obstruction alone, however, cannot be the entire explanation because papilledema does not necessarily occur with extreme venous congestion produced experimentally<sup>5</sup> and does not always occur with clinical complete venous obstruction. Also, if venous obstruction were the entire explanation, one would expect its effects to be applied not just at the disc but equally over the whole retina in which the circulation is terminal.

- b. obstruction of a normal flow of tissue fluid centripetally from the eye along the optic nerve.<sup>12,13</sup>

This theory maintains there is a normal stream of tissue fluid from the disc along the nerve and that interruption of this results in stasis and edema. Some have thought this fluid to be intra-ocular fluid; others have thought it to be tissue fluid of the nerve tissue itself.

- c. Cerebro-spinal fluid forced under pressure into the optic nerve.<sup>14</sup>

This theory maintains that cerebro-spinal fluid is forced along the perivascular sheaths in the center of the nerve to the disc. Most of the experimental work to show this, however, has given negative results.<sup>5</sup>

- d. edematous process of the brain spreading forward to include the disc.

Papilledema here is considered only an expression of a general cerebral edema. To support this is the brain edema which is known to occur locally with a brain tumor and generally in states of malnutrition. Also, in support, is the experiment which produces papilledema on the side in which distilled water is injected into the carotid, and an excavation of the disc on the side in

which 10% saline is injected.<sup>5</sup> Furthermore, it has been shown that the water-binding capacity of the retina is less than that of the brain and optic nerve.<sup>15,16,17</sup> This would explain the limitation of the process to the neighborhood of the disc. The papilledema of hypertension and uremia have also been explained on this basis of a coexistent brain and optic nerve edema.

The following summarizing statements may then be made on the pathogenesis of papilledema:<sup>5</sup>

- a. Increase in intra-cranial pressure alone<sup>18</sup> is probably not sufficient to account for the occurrence of papilledema. Most experiments in this direction have produced nothing more than venous engorgement.<sup>19</sup>
- b. Venous blockage probably plays a crucial part and the point of pressure is very likely in the inter-vaginal space.<sup>11</sup>
- c. An additional factor is necessary. A possibility for this is the pushing of cerebro-spinal fluid into the nerve-head or the obstruction of a flow of tissue fluid back along the nerve. A likely explanation presented by Duke-Elder is an alteration of the water binding properties of the tissues caused by the venous stasis.<sup>5</sup>

The pathology of papilledema<sup>4,5,10,11,13,20,21</sup> consists of simple edema of the optic nerve head with an edematous swelling of the nerve fibers and infiltration of all the tissues with fluid. This area of edema is fairly well limited, extending from the retina a little beyond the margin of the optic disc to end fairly abruptly near the point where the retinal vessels leave the nerve. The lamina cribrosa, especially the less dense anterior part, is bowed forward. The physiological cup is smaller or completely obliterated and the tissues of the disc project into the cavity of the eye displacing the retina laterally and throw-

ing it up into small folds. The veins and capillaries are invariably distended and hemorrhages are commonly seen on the disc and in the nerve fiber layer immediately surrounding the disc. Hemorrhage does not usually occur within the optic nerve itself. Where the central vein enters the vaginal space it is usually found to be greatly compressed. The sub-arachnoid space of the nerve is distended and ends anteriorly at the sclera in a bulging cul-de-sac. In severe acute and in long standing cases the nerve fibers develop varicosities. These varicosities are later separated from the nerve fibers and are then described as cytooid bodies.<sup>3</sup> In later stages there is proliferation of glial tissue which gives to the disc a peculiar grayish appearance. Signs of inflammation are noticeably absent throughout. The scanty perivascular infiltration occasionally found is consistent with a secondary reaction to the destructive and degenerative changes occurring in the nerve.

## 2. Papillitis

As stated previously, the term, optic neuritis, is used to describe involvement of the optic nerve as the result of inflammation, demyelination, or degeneration. On a basis of pathology this involvement is described in three principal types:

### a. perineuritis

This is an inflammatory involvement of the optic nerve sheaths (meninges) from an extension of meningitis. A majority of such cases show coincident or subsequent involvement of the stem of the nerve.

### b. axial neuritis

The papillo-macular bundle in the nerve is here involved.

### c. transverse neuritis

The entire cross-section of the nerve shows involvement.

To indicate the precise site of such involvement the terms retrobulbar neuritis and papillitis (intra-ocular neuritis) are used. A papillitis then may be an expression of an involvement of the papillo-macular bundle at this level, a periaxial involvement, the entire cross-section of the optic nerve, or only of the optic nerve sheaths immediately adjacent to the eye.<sup>4</sup>

The etiology of optic neuritis of all types is classified by Walsh<sup>4</sup> as follows:

## 1. Local inflammatory conditions

- a. Intraocular: retinitis and choroiditis, sympathetic ophthalmia, tuberculosis, syphilis, etc.
- b. Orbital inflammation and tumors.
- c. Sinusitis
- d. Meningitis: syphilis, tuberculosis, cerebrospinal meningitis.

## 2. Demyelinating Diseases

- a. Disseminated sclerosis
- b. Disseminated encephalomyelitis, spontaneous, or following infectious diseases.
- c. Neuromyelitis optica
- d. Encephalitis periaxialis diffusa (Schilder's disease)
- e. Pertussis encephalopathy
- f. With polyneuritis.

## 3. Endogenous Toxins

- a. Acute infectious diseases: influenza, malaria, pneumonia, la grippe, measles, acute anterior poliomyelitis, etc.
- b. Septic foci: teeth, tonsils.
- c. Metabolic diseases: diabetes, anemia, puberty, pregnancy, lactation, hyperemesis gravidarum, pella, beriberi, etc.

## 4. Poisons, including the Toxic Amblyopias

## 5. Hereditary Optic Neuritis (Leber's

Disease)

## 6. Unknown Etiology

A great majority of the cases in general are now considered due to disseminated sclerosis,<sup>22</sup> and the usual type of involvement is that which exhibits a selective affinity for the papillo-macular bundle giving characteristically a central scotoma in the visual field.

Optic perineuritis is relatively infrequent and is usually present in the purulent form arising as an extension from the cerebral meninges.<sup>23,24</sup> The rare localized exudative (non-suppurative) form has been described most often as a result of syphilitic meningitis.<sup>4</sup>

Purulent involvements<sup>4,25</sup> of the optic nerve are rare but may occur (1) as an extension from a purulent meningitis spreading to the nerve from the nerve sheaths, (2) from orbital suppuration, (3) as an extension of a purulent endophthalmitis, and (4) as a result of metastatic abscess formation.

Total transverse optic neuritis gives rise to amblyopia or amaurosis affecting the entire field. When the parts of the nerve are affected in different degrees, the papillo-macular bundle is usually found to be most severely affected. Such a transverse involvement would, therefore, be considered as originating from an axial neuritis.<sup>4</sup>

The pathology of optic nerve<sup>4,5</sup> inflammations consists of proliferative changes in the interstitial tissues followed by degenerative changes in the neural tissues. Both are invariably present but vary considerably in their predominance with the type and severity of the inflammation. Edema of all tissues occurs first and then there is a dense infiltration of the septa with leucocytes, lymphocytes, and plasma cells. The connective tissue septa of the nerve are thus thickened as new vessels and granulation tissue are formed. This change in addition to the edema and subsequent fibrosis and shrinkage are responsible for the compression and strangula-

tion of nerve fibers leading to degeneration. The degenerated neural tissue is replaced by glial tissue.

## 3. Pseudo-neuritis

This congenital anomaly of the disc is probably an ectodermal deformity depending on neuroglial overgrowth.<sup>5</sup> A large excess of glial tissue is present at the disc with a heaping up of the nerve fibers to form an elevation. It occurs usually in small hyperopic eyes<sup>26</sup> and also may occur familiarly<sup>27</sup>, when it is known as "congenital familial pseudo-neuritis".<sup>4,28,29,30</sup>

### Clinical Diagnosis

#### 1. Papilledema.<sup>4,5,31,32</sup>

The symptoms and signs associated with papilledema are variable and are largely determined by the etiologic factors responsible for the development of it. Much of the symptomatology then does not concern vision or visual fields.

Headache, therefore, is usually one of the earliest symptoms of increased intra-cranial pressure. It is possible, however, to have pronounced increase in the intra-cranial pressure without headache. The cause of this headache is fairly well established as stretching of the meninges.

Nausea, vomiting, bradycardia, difficulty in swallowing, and eventual failure of respiration are associated with high-grade increased intra-cranial pressure and may all be explained as due to herniation of the medulla into the foramen magnum.

The diplopia which is often associated with papilledema from increased intra-cranial pressure is explained on the basis of compression of the sixth nerve on each side by one of the transverse branches of the basilar artery.

Loss of consciousness, generalized motor rigidity, and pupillary dilatation are considered terminal pressure effects

on the cerebral cortex and third cranial nerve.

The ocular symptomatology of papilledema is frequently very vague and may remain slight even when the swelling is very great and long established. Transient attacks of blurred vision or even blindness occur frequently with pronounced papilledema. Such attacks usually last only a few minutes. Their cause has not been established, but suggestions of pressure on the chiasm from intermittent internal hydrocephalus, sudden compression of the optic nerves in the optic canals, and spasm of the retinal arterioles have been offered. The visual acuity, except during these spells of transient blurring, is characteristically normal or near normal during the early stages. With long-standing papilledema atrophy begins to develop and then visual symptoms become increasingly evident.

Perimetrically the earliest sign is a concentric enlargement of the blind spot. The area corresponds roughly with the degree of edema and is due to the increase in size of the disc and the lateral displacement of the retina. It must be remembered, however, that the normal blind spot varies in size in normal eyes and therefore enlargement must either be pronounced, or have been shown in successive fields to have increased, before the sign is in itself significant. The edema may extend into the surrounding retina and toward the macular area. When the macular area is thus involved, a relative central scotoma develops and central vision is diminished. Concentric contraction of the peripheral field begins with atrophy of the nerve. As the atrophy progresses the contraction increases with it, but is more rapid on the nasal side than on the temporal. The field then in the later stages becomes small, more or less centrally located, and embraces the blind spot. Permanent blindness with a widely dilated immobile pupil is the usual end result of an unrelieved papilledema which has gone on to complete atrophy.

The ophthalmoscopic diagnosis of early

papilledema is based on a combination of several minimal changes from normal:

a. Hyperemia of the disc

Most authorities agree that increased redness of the disc is one of the earliest signs. This in itself, however, is unreliable since the color of the normal disc varies within limits and there is a tendency toward hyperemia in hyperopia and pallor in myopia. The sign, nevertheless, is of some importance, especially when the examiner knows that the color of the discs has changed.

b. Blurring of the disc margins

The slight haziness and blurring of the disc margins appears first at the upper and lower poles, spreads then to include the nasal margin, and appears last at the temporal margin. This sign again is not diagnostic of papilledema because blurring of the disc margins occurs in a high percentage of normal hyperopes and in a smaller percentage of normal emmetropes.

c. Blurring of the details of the physiological cup.

This is considered one of the earliest signs of papilledema and in this region also is often seen a veil-like graying and streaking along the vessels. Again there is a wide variation in physiological cupping and streaking of the vessels in this region is occasionally seen in normal eyes.

d. Turgidity of the retinal veins.

The slight but perceptible overfilling of the veins is considered by some the most important single evidence of early papilledema. The normal vein-to-artery size ratio of 3 to 2 is thus upset toward a ratio of 2 to 1.

e. Absence of venous pulsation on the disc.

When there is absence of venous pulsation at the disc in addition to overfilling of the retinal veins, the evidence for papilledema is quite strong. It becomes still stronger when the pulsation cannot be started by light finger pressure on the globe.<sup>4,5</sup> Heavier finger pressure on the globe raises the intra-ocular pressure to a level above that of the intra-cranial pressure and venous pulsation will then be initiated.<sup>2</sup>

f. Few small hemorrhages on or adjacent to disc occasionally.

After a period of one to two weeks in the average case from tumor, the signs become more definite and unmistakable:

- a. Partial or complete obliteration of the physiological cup.
- b. Definite blurring of the disc margins.
- c. Color of the swollen hyperemic disc approaches that of the surrounding fundus.
- d. Often a grayish tinge to retina surrounding the disc.
- e. Further engorgement of the retinal veins.
- f. Vessels on and immediately surrounding the disc often are partially "lost" in the edematous tissue.
- g. Hemorrhages as linear streaks on or around the disc. Occasionally there may be massive subhyaloid hemorrhages.
- h. Spots of exudate on or about the disc.
- i. Edema of the disc often to a "mush-

rooming" of it. Measurements of 6 to 8 diopters in extreme degrees (3 diopters corresponds to 1 mm. of actual protrusion).

- j. Macular figure (fan or star) occasionally. Histologically these have been shown to be due to edema vesicles under the internal limiting membrane of the retina passing along the radiating nerve fibers of the macula.<sup>3</sup> The macular star may resemble very closely that of so-called albuminuric retinitis. In papilledema, however, the figure is usually fan-shaped and extends between the disc and the fovea.<sup>5</sup>

Papilledema which subsides leaves little or no permanent changes. However, if it has persisted for long the signs of secondary atrophy usually result. This is due to destruction of the nerve fibers and their replacement by glial tissue. The disc then shows decreased vascularity, pallor, and a sinking of its prominence. The arterioles become contracted and their sheaths are thickened.

## 2. Papillitis

The outstanding symptom of papillitis and all other types of optic neuritis is usually loss of vision. Typically this loss is of central vision from an involvement of the relatively delicate papillo-macular bundle of fibers. The most significant change in the visual fields, then, is a central scotoma which may be large or small and relative or absolute depending on the extent and degree of involvement. Variations from this loss of central vision are, nevertheless, very common. There may be a peripheral field defect from a periaxial involvement of the nerve, a total loss of field from a transverse nerve involvement, or a perfectly normal field from an involvement of the perineural sheaths alone. Other symptoms and signs which may be present are: (1) pain in and behind the eye, especially on movement,<sup>33</sup> (2) sluggishness of pupillary response

roughly paralleling the reduction of visual acuity,<sup>4,5</sup> and (3) lowering of dark adaptation.<sup>5</sup> As a general rule the symptoms come on quite suddenly, last a short period of 1 to 4 weeks, and recovery of vision may be very complete.

The ophthalmoscopic appearance of papillitis most closely resembles that of papilledema. Also, the loss of vision may occur before changes in the optic fundi become visible. The following changes may be listed:

- a. Early hyperemia of the disc.
- b. Overfilling of the retinal veins.
- c. Blurring of the disc margins.
- d. Partial or total obliteration of the physiological cup.
- e. Edema of the disc.

As a rule this is not more than 2 diopters. Occasionally, however, the inflammatory lesion is located just behind the lamina cribrosa producing a non-inflammatory passive edema, a true papilledema, of 6 or more diopters.<sup>34</sup>

- f. Hemorrhages, usually of the striate variety, commonly on and close to the disc.
- g. Exudates close to the disc.
- h. Commonly a cloud of opacities in the posterior vitreous making the entire picture hazier.
- i. Occasionally an involvement of the surrounding retina (neuro-retinitis).

A star-figure in the macula may be present with this development.

As a rule these ophthalmoscopic changes subside after a short period and complete or almost complete recovery of vision occurs synchronously. No trace of pathological change may be evident after a few weeks but most commonly some degree of post-neuritic atrophy is seen. This is characterized by a grayish appearance to the disc due to the presence of a variable amount of fibrous tissue.

The lamina cribrosa is obscured, the physiological cup is obliterated, the disc margins are indefinite, and the vessels at the disc may show white perivascular sheathing. This permanent picture is often very difficult to distinguish from the atrophy secondary to a severe papilledema.

### 3. Pseudo-neuritis

This congenital anomaly of the optic disc is usually an incidental clinical finding with no associated symptomatology. A diagnosis is frequently difficult under these conditions but is even more difficult when a coincidental complaint of headache or a slight loss of vision is present. Only after a long period of observation without ophthalmoscopic change, after visual fields have been repeatedly found to be normal, and when the intra-cranial pressure is found to be normal can a diagnosis be made with any degree of certainty.

The clinical characteristics of pseudo-neuritis may be listed as follows:

- a. Normal or near normal vision.
- b. Normal visual fields.
- c. No headaches, eye pains, etc.
- d. Hyperopia present in high percentage of cases.
- e. Condition often present as a familial characteristic.
- f. Non-progressive ophthalmoscopic picture:

- (1) Blurring and swelling of nasal margin of disc in cases of lesser degree; marked swelling of disc (as much as 10 diopters<sup>2</sup>) in cases of pronounced degree.

- (2) Small or absent physiological cup,
- (3) Vessels of normal calibre bend as they pass from the swollen disc to the lower level of the retina.

- (4) Tortuosity of retinal vessels common.

- (5) Absence of hemorrhages and

- exudates.  
 (6) Absence of venous engorgement.  
 (7) Normal venous pulsation at disc usual.  
 g. Normal intra-cranial pressure.

#### 4. Differential Diagnosis

The clinical differentiation of papilledema, papillitis, and pseudo-neuritis may then be summarized in the following table:<sup>35,36,37,38,39</sup>

	<u>Papilledema</u>	<u>Papillitis</u>	<u>Pseudo-neuritis</u>
Nature	Progressive until relieved. Usually bilateral.	Temporarily progressive. Usually unilateral.	Congenital and non-progressive. Usually bilateral.
Degree of disc swelling	Frequently more than 2 diopters	Rarely over 2 diopters	Great variability. Slight swelling most common.
Venous engorgement and hemorrhages	Usually marked	Less marked	Absent
Venous tortuosity	Usually present	Usually present	Commonly present
Venous pulsation at disc	Absent	May be present	Usually present
Pain on pressure or movement of eyeball	Absent	Present	Absent
Loss of vision	Minimal. Late in onset. Usually slowly progressive until condition relieved	Marked. Early and abrupt in onset	None
Field defect	Enlargement of blind spot early. Concentric contraction late	Central scotoma typically	None
Recovery of vision	May be complete if condition relieved	May be complete	----

When these points are inadequate for differentiation, other tests and a longer period of observation become necessary. The demonstration of normal or increased intra-cranial pressure often becomes the differentiating point between papillitis and papilledema.

Ophthalmoscopically, optic perineuritis and papilledema are indistinguishable. Perineuritis, however,

is quite rare and its diagnosis must necessarily be provisional until some therapy produces changes which seem to establish it.<sup>4</sup>

Occasionally obstruction of the central retinal vein becomes a problem in differentiation from papilledema associated with increased intra-cranial pressure. This is particularly so when the obstruction is old and most of the

retinal hemorrhages from it have disappeared. Central vein obstruction, however, occurs almost always unilaterally and is characterized by profuse and extensive retinal hemorrhages with relatively little edema of the disc and surrounding retina.

Lastly, marked refractive errors, particularly astigmatism, may produce the appearance of blurring of the disc margin and must be differentiated from the above entities. Varying the lens in the ophthalmoscope, however, usually makes the margin clear and establishes the condition.

#### Summary

The etiology, pathology, and clinical characteristics of papilledema, papillitis, and pseudo-neuritis have been discussed.

In practice, a differentiation of these conditions is frequently very difficult. The history, clinical examination, ophthalmoscopic appearance, and visual acuity may be inconclusive. The study of central fields of vision then becomes of greatest importance. To facilitate earliest possible treatment for intra-cranial disease, all cases of nerve-head swelling should be considered the result of increased intra-cranial pressure until proven otherwise.

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### III. MEDICAL SCHOOL NEWS

#### Dr. Weaver Accepts New Post

Dr. Myron M. Weaver, Assistant Dean of Medical Sciences and Associate Professor of Medicine and Public Health, has recently announced that he has accepted a post as Dean of the Medical School at the University of British Columbia, Vancouver. This University has not had a medical school up to the present, and it will be Dr. Weaver's responsibility and opportunity to have the leading role in creating a new school of medicine.

Dr. Weaver has contributed untiringly to the teaching activities of the Medical School and its administration. In addition to this, he has been very active in the medical affairs of this state, working diligently on various committees of the Minnesota State Medical Association. He was active in the work which ultimately lead to the formation of the Minnesota Medical Service, Inc., Minnesota's Blue Shield plan for prepaid medical care.

All of his many friends here at the University will wish to congratulate him on this well deserved honor and wish him God's speed when he leaves to assume his new duties on July 1 of this year.

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#### Dr. Anderson Attends Conference

Dr. Gaylord W. Anderson, Director of the School of Public Health at the University, is participating this week in the Inter-American Conference of Health and Sanitation Officers. Dr. Anderson will attend as a member of the staff of consultants with the Division of Health and Sanitation of the Institute of Inter-American Affairs. Health and Medical officers from 14 American countries will participate. The conference which is being held in Quito, Ecuador, will discuss institute affairs and plan the division's future program.

#### Biographical Briefs Pediatrics Chief

Irvine McQuarrie was born in St. George, a small town in southwestern Utah. He attended the University of Utah, entering in the School of Mines. His interest in biological sciences led him to transfer from Mining to a Biology major, and he received his Bachelor of Arts degree in 1915. As a graduating senior, he was awarded the competitive Willard E. Thompson Scholarship. He utilized this two-year grant by going directly to the University of California where he did graduate work in biochemistry. During four years of study at the University of California, he was a fellow of the Hooper Foundation for Medical Research and an assistant in Pathology. This University granted him a Ph.D. in Biochemistry in 1919.

A cross-country trip followed and Irvine McQuarrie was soon living in Baltimore, attending Johns Hopkins University Medical School. Because of his work in biochemistry and pathology and by attending all the summer sessions, he was able to receive his M.D. in 1921.

Dr. McQuarrie went from Hopkins to the Henry Ford Hospital in Detroit where he served from 1921 to 1924, going up the academic scale from intern to resident in the Department of Medicine. At that time, there was no Department of Pediatrics at Henry Ford Hospital. The care of infants and children was covered by the medical department. The academic year 1924-25 found Dr. McQuarrie in the Ivy League as Instructor in Pediatrics at Yale University. He returned to Henry Ford Hospital in 1925-26 to head the newly formed Department of Pediatrics. He served the Department of Pediatrics at the University of Rochester from 1926 to 1930 when he came to the University of Minnesota as Professor and Head of the Department of Pediatrics.

### Pediatrics Continuation Course

A continuation course in Pediatrics will be presented at the Center for Continuation Study on April 7, 8, and 9. The course which is being presented under the direction of Dr. Irvine McQuarrie and Dr. John Adams of the Department of Pediatrics will be devoted to allergic problems in pediatrics and infectious diseases. Distinguished visiting physicians who will contribute to the course as faculty members include Dr. Amos Christie, Vanderbilt University; Dr. Jerome Glaser, University of Rochester School of Medicine; Dr. Robert L. Jackson, University of Iowa; Dr. Karl H. Pfuetze, Medical Director and Superintendent, Mineral Springs Sanatorium; and Dr. Arvid J. Wallgren, Gothenburg, Sweden.

Clinical and full-time members of the Medical School faculty and Minnesota Department of Health will complete the faculty for the course.

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### Bids on New Student Health Service Announced

The University has recently announced plans for a new Student Health Service building on the main campus of the University. The building which is estimated to cost in excess of \$750,000 will be erected just across the street from the out-patient wing of the University Hospital and just south of the Botany Building. The building will be four stories high and will contain examining rooms, doctors' offices, a large eye, ear, nose and throat clinic, a dental clinic, an x-ray department, and waiting lounges. No in-patient beds will be provided in the new building since the Health Service will retain its bed space on the fourth and fifth floors of the present Health Service wing of the University Hospitals. Cost of the structure will be made from Health Service earnings.

### McClure Gift for Medical Research

The Medical School will receive a gift of approximately half a million dollars from the estate of Silas McClure, Minneapolis businessman who died February 16 at the age of 83. Mr. McClure was the organizer of the Monarch Range Company. He came to Minneapolis in 1921 as president of the Electric Machinery Manufacturing Company.

His will directs that the assets received from the estate be used by the University in the promotion of medical research. Before his death, he had given the University grants in memory of his wife, Katherine Esgen McClure.

Expressing the University's gratitude for the gift, President J. L. Morrill said, "The very generous bequest provided by Mr. Silas McClure to the University of Minnesota for medical research is further evidence of the general acceptance of the high professional competence of University scientists. The University is profoundly grateful."

In commenting on Mr. McClure's gift to the Medical School, Dean Harold S. Diehl stated, "An unrestricted fund for medical research, such as Mr. McClure has made available, will be particularly valuable. It can be used for the purchase of needed scientific equipment or to provide the technical assistance and supplies necessary to explore new scientific ideas and develop new research programs. This is truly the pioneer work of scientific prospecting upon which medical progress must depend. Mr. McClure's generous bequest will be used to underwrite such prospecting in better health for the people, not only of Minnesota but of the world."

### New Minn. Medical Foundation Members Carl O. Rice, M.D., 1635 Medical Arts

Building, Minneapolis, Minn.  
Hillard H. Holm, M.D., Glencoe, Minn.  
W. H. Condit, M.D., 1009 Nicollet Ave.,  
Minneapolis, Minn.  
H. W. Havel, M.D., Jordan, Minn.