Rendu-Osler-Weber syndrome and ocular manifestations in hereditary hemorrhagic telangiectasia

Daniel A. Jenisch
Pacific University
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Abstract
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RENDU-OSLER-WEBER SYNDROME
AND
OCULAR MANIFESTATIONS IN
HEREDITARY HEMORRHAGIC TELANGIECTASIA

BY

DANIEL A. JENISCH

A thesis submitted to the faculty of the
College of Optometry
Pacific University
Forest Grove, Oregon
for the degree of
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Advisor:

Salisa K. Williams, O.D.
RENDU-OSLER-WEBER SYNDROME AND
OCULAR MANIFESTATIONS IN
HEREDITARY HEMORRHAGIC TELANGIECTASIA

Submitted by: DANIEL A. JENISCH

Advisor: SALISA K. WILLIAMS, O.D.
ABOUT THE AUTHOR

The author was born in the city of Bend, Oregon in 1957. He received his Bachelor's Degree in Criminal Justice from Washington State University in May of 1980. A second degree in General Science was conferred in May of 1986 from University of Oregon. This thesis was produced as a partial requirement for the fulfillment of the Doctor of Optometry Degree from Pacific University College of Optometry to be awarded on May 17, 1992.

The author's future plans include practicing full-scope optometry in the state of Washington as an associate of a practice.
ABSTRACT

The relatively rare syndrome of Rendu-Osler-Weber and the associated hemorrhagic telangiectasia present with various ocular signs, such as telangiectases of the lids, conjunctiva, and retina. This syndrome also presents with non-ocular hemorrhagic telangiectases and is of a hereditary origin. As a primary care provider, the optometrist may be the first health care professional to examine the patient with Rendu-Osler-Weber syndrome or hereditary hemorrhagic telangiectasia. Although this syndrome is relatively rare, the eye care practitioner should be aware of specific systemic complaints as well as ocular manifestations since these can mimic several other ocular diseases and abnormalities. This paper discusses ocular and systemic manifestations, differential diagnoses, and management. The goal of this paper is to provide a comprehensive report of Rendu-Osler-Weber syndrome.

KEY WORDS

Telangiectasia, atavism, dominant inheritance, epistaxis, arteriovenous malformation, neovascularization, and filamentary keratitis.
I would like to thank Dr. Salisa Williams for her guidance, ideas, inspiration, and perseverance. Working with her was an honor and pleasure.

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INTRODUCTION

The original descriptions of hereditary hemorrhagic telangiectasia (HHT), or Rendu-Osler-Weber disease (R-O-W disease), were published nearly a century ago (Osler, 1901; Rendu, 1906; Weber, 1907; and Hanes, 1909). Its various manifestations have been illustrated in medical and ophthalmological journals. The scope of these reports tended to be limited. The goal of the present report is to combine the knowledge we have of HHT, with systemic and ocular reports consolidated into one review, with an emphasis on the ocular manifestations.

HHT is described as a generalized vascular dysplasia characterized by widespread dermal, mucosal, and visceral telangiectases (dilated capillary endings) associated with recurrent bleeding. Epistaxis (nosebleeds) and gastrointestinal bleeding are particularly common.

Ocular signs have been reported in patients with hereditary hemorrhagic telangiectasia. The most prevalent ocular abnormalities are conjunctival telangiectases, with only a few reported cases of intraocular involvement. HHT is highly variable in its expression. It is usually recognized as a "classic tried" of telangiectasia, recurrent epistaxis, and a family history of the disorder. However, owing to variability in the type, location, and number of randomly distributed vascular
malformations, affected persons may be asymptomatic or present at any age with a wide range of clinical manifestations.\(^2\)

The symptoms are the result of bleeding and the consequent anemia, in general becoming more severe with advancing age. Some of the more frequent signs and symptoms reported by patients relative to HHT are epistaxis, dyspnea on exertion, and gastrointestinal bleeding. Specifically, the patient may feel weak, dizzy, and tired after a prolonged nosebleed, or as a result of bleeding heavily from the gastrointestinal tract.

Symptoms related to the eyes are relatively rare, and can range from bloody tears to acute external hemorrhage. Profuse bleeding from telangiectatic vessels in the palpebral conjunctiva can also result in a heavy loss of blood and result in the same aforementioned symptoms.

Although the disease entity has been known by various names, the term most widely used in the United States is hereditary hemorrhagic telangiectasia. Other terms frequently used are Rendu-Osler-Weber disease, Goldstein's heredofamilial angiomatosis, familial hemorrhagic angiomatosis, and just simply, Osler's disease. Rendu, in 1896, was the first to recognize the symptom complex and called attention to the association of familial nosebleeds and multiple telangiectasis. Osler, in 1901, described the entity in an extensive report, and Weber, in 1907, added additional details to complete the information as we know it today.
EPIDEMIOLOGY AND INCIDENCE

HHT occurs in all races, with an estimated frequency of one or two per 100,000 people in the European population and considerably less in other races.\(^3\) HHT is a rare disease.

The incidence of HHT, as reported by Wintrobe, in specific population groups is listed in the order given: 1) Anglo-German, 2) Latin, 3) Scandinavian, and 4) Jewish.\(^4\) Only one case was reported in the African-American population. However, in 1954, Smith and Lineback reported nine cases of HHT in one African-American family.\(^1\)

Hereditary hemorrhagic telangiectasia is a genetic disorder transmitted as an autosomal dominant trait. If one of the two parents had HHT, the offspring would have a 50% chance of contracting this disease. One biographic study showed that 244 recorded families which included 648 males and 703 females (a total of 1,351 affected persons) had been reported by 1950. Of 463 individuals who transmitted the defect, 243 were female and 220 male. This establishes that the disease, which is transmitted as a mendelian dominant trait, affects both sexes equally.

Most patients with HHT report similarly affected relatives; however, in 20 percent of cases, there is no family history of either recurrent bleeding or telangiectasia. This skipping of generations, or atavism, is not admitted to by dominant inheritance.\(^5\) HHT is not, as in hemophilia, sex-linked. It is transmitted by both sexes directly to both daughters and sons. Schoen proposes that the
apparently normal and healthy individual who passes on the trait to
his/her offspring may, nonetheless, have the disease in a mild or
abortive form.\textsuperscript{5} The individual may, for instance, have unnoticed
lesions in the nose or elsewhere, without having hemorrhages of
such frequency or severity as to call them to attention.\textsuperscript{5} It is likely
that in a rare condition, such as HHT, where urgent manifestations
(signs/symptoms of HHT) are often deferred until late in life, its
existence would occasionally be overlooked or be mistakenly
attributed to some other cause. In childhood, the telangiectases are
usually not present, or if present, may not be discovered.

A syndrome of familial epistaxis without any apparent sign
of telangiectases was reported in 1926 and 1927.\textsuperscript{6} This was the
initial diagnosis until nasopharyngoscopy revealed multiple
telangiectases. Telangiectases may be absent on external inspection
though several may be present in the posterior nasopharynx. This
may explain why HHT can occur in the absence of an undiagnosed
positive family history.

Lesions, that have been reported to occur in almost any portion
or organ of the body, usually make their appearance during the
second decade but, occasionally, cases have been reported in which
the lesions were seen much earlier.\textsuperscript{7} The earliest age of onset was
reported by Dolowitz, in 1953, involving a case of a three - month -
old child.\textsuperscript{7} Usually, the onset of symptoms is at puberty, with a
notable gain in the size and number of the lesions as the years
advance. By the fourth decade of life, the signs and symptoms have
reached a maximum and, at this time, control is frequently an
annoying or bothersome medical problem.
Longevity is not inevitably reduced nor is quality of life necessarily impaired. Peery states that the limited mortality data suggest that fewer than 10 percent of all affected persons ultimately die of complications directly attributable to the trait.

Some authors have published reports of increased occurrence of blood group 0 in patients with HHT. One study compared the blood group pattern of HHT patients both with and without gastrointestinal telangiectases, and compared the group pattern of the total HHT group with that of the background (normal) population.

The blood group apportionment of the HHT patients with gastrointestinal telangiectases did not differ from that of HHT patients with no signs of GI telangiectases, but blood group 0 occurred significantly more frequently in patients with HHT than in the comparative background population.8

Table 1 summarizes the results of Vase and Grove’s study published in 1986:8

**TABLE 1**

<table>
<thead>
<tr>
<th>Distribution of ABO Blood Groups</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>Patients With HHT and GI Telangiectases</td>
<td>28</td>
</tr>
<tr>
<td>Pts. w HHT &amp; No Evidence of GI Bleeding</td>
<td>93</td>
</tr>
<tr>
<td>Background Population</td>
<td>26,877</td>
</tr>
</tbody>
</table>
SYSTEMIC MANIFESTATIONS

A. EPISTAXIS

Recurrent mucous membrane hemorrhage occurring spontaneously or precipitated by minor trauma, is the prominent clinical feature of HHT. Epistaxis is not only the most common, but prevalently the first hemorrhagic event in HHT. Possibly, this is due to the ready accessibility of the nasal septum to minor trauma.

The pattern of epistaxis in HHT is variable. According to Peery, approximately one third of affected patients have mild nosebleeds, one third have moderate bleeding necessitating outpatient assistance, and one third have incapacitating hemorrhages requiring transfusions and hospitalization.2 The established bleeding pattern remains stable and chronic in about half of the patients, with the remainder showing progression (up to 50 percent) or spontaneous regression (up to 50 percent).2 There appears to be no correlation between the duration and severity of epistaxis.2

According to Saunders, a nosebleed which begins about puberty, is the cardinal sign of HHT.9 Repeated bleeding from small nasal telangiectases may commence during childhood before cutaneous lesions have achieved detectable size and number. Vase and Grove state the median age of onset of epistaxis is 11 years.8
Epistaxis may occur daily, several times a day, or sometimes only a few times each year, as unpredictable and annoying minor hemorrhages. A severe hemorrhage may also occur several times within a year following minor hemorrhaging.

**B. GASTROINTESTINAL BLEEDING**

GI hemorrhage is the second most common presentation, behind the occurrence of epistaxis, being the initial symptom in 25% and occurring at some time in 44% of patients with HHT. Some investigations have shown that GI bleeding occurs in 13% - 30% of patients with HHT.

The primary gastrointestinal manifestation of HHT is painless bleeding from arteriovenous malformations and telangiectases in the upper or lower bowel. An increased occurrence of duodenal ulcer (15 percent) is reported in HHT but the pathophysiologic relationship between the two disorders remains to be established.

In contrast to nosebleeds, GI bleeding in HHT is typically delayed until the fourth or fifth decade, though the reason for this delay is unknown. The bleeding pattern is evidenced by chronic, recurrent hemorrhage that tends to be progressive in the majority of cases.
C. TELANGIECTASES

In 1909, Hanes defined HHT disease as a "hereditary affection manifesting itself in localized dilatations of the capillaries and venules forming distinct groups of telangiectases which occur upon the skin of the face, nasal and buccal mucous membranes (Figures 1, 2, & 3), and give rise to profuse hemorrhage either spontaneously or as a result of trauma."\(^{10}\)

Telangiectases, which appear to originate from postcapillary venules and capillaries, are dilated channels lined by a single layer of endothelium attached to a continuous basement membrane.\(^2\) Bleeding from telangiectases occurs in spite of normal platelet function tests and hemostasis and is therefore thought to be related to local irregularities within the malformed vessels.\(^2\) Defects in endothelial junctions, endothelial cell degeneration, and weakness of the perivascular connective tissue are proposed as major components jeopardizing the integrity of these vascular lesions.\(^2\)

The maintenance offered by tissues enclosing telangiectases also influences their bleeding tendencies. For example, cutaneous lesions rarely bleed but nasal telangiectases regularly do, though both may be exposed to trauma. Nasal telangiectases may bleed with the slightest trauma or even during sleep.\(^6\) Unquestionably the skin, being the tougher organ, offers more supportive protection than the relatively fragile mucous membranes.

The most characteristic cutaneous lesion is a small (1 to 3 mm) punctiform, violaceous, non-elevated telangiectasis.\(^6\)
Figures 1, 2, & 3
Cutaneous telangiectases are obviously true vascular formations, not blood extravasations.\textsuperscript{11} They blench with pressure, unless a hemorrhage has recently occurred, and regain their color when the pressure is removed.\textsuperscript{12} Cutaneous telangiectases in HHT patients often do not become apparent until the second or third decade of life.

Telangiectases have been known to occur in almost every organ of the body in HHT patients (Table 2 & Table 3). These lesions appear in the following sites in increasing order of frequency: scalp and ears, conjunctiva, under the nails, fingers, trunk (Figure 4), skin of face, tongue (Figure 5), palate (Figure 6), buccal mucosa, gingiva, inner surface of lips (Figures 7, 8, & 9), and nasal mucous membrane (Figure 10). Telangiectatic lesions are also commonly encountered in the eyelids, spinal cord, brain, meninges, bladder, kidney, uterus, respiratory tract, and stomach (Table 4).\textsuperscript{6}
Figure 2A. — Angiomatosus vascular lesion on the hard palate, including several areas of telangiectatic lesions.

Figure 7. — Telangiectatic mats are present on the patient's lips and tongue.

Figure 8. — Multiple telangiectatic lesions of upper lower lips.
In a study done in the Haut-Jura, near Lyon, France, where HHT is endemic, Piachu et al conducted an age-related clinical profile of hereditary hemorrhagic telangiectasia in an epidemiologically recruited population. Of 1,270 cases recruited by epidemiological survey 324 patients with HHT were studied. This study found 25% (or 80/324) of patients with visceral involvement. This same study determined 15% (or 48/324) of patients had gastrointestinal involvement, 8% (or 27/324) of patients had hepatic involvement, 4.6% (or 15/324) of patients had pulmonary involvement, and 4% (or 13/324) of patients had CNS involvement. Some of the patients had evidence of two (21/80) or three (2/80) organ involvements.
TABLE 2

Telangiectasia: Detailed Accounts of Mucocutaneous Involvement of the Head

<table>
<thead>
<tr>
<th>Involved area</th>
<th>Percentage of patients showing involvement in each site</th>
<th>Incidence of site involvement</th>
<th>Mean no. lesions per involved area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower lip</td>
<td>39</td>
<td>11.5</td>
<td>5</td>
</tr>
<tr>
<td>Nose</td>
<td>37</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Tongue</td>
<td>33</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Cheeks (skin)</td>
<td>31</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Ears</td>
<td>13</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Palate</td>
<td>12.9</td>
<td>2.5</td>
<td>5</td>
</tr>
<tr>
<td>Forehead</td>
<td>5</td>
<td>1.5</td>
<td>4</td>
</tr>
<tr>
<td>Gums</td>
<td>5</td>
<td>0.7</td>
<td>3</td>
</tr>
<tr>
<td>Eyelids</td>
<td>4.3</td>
<td>0.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Chin</td>
<td>3.7</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Cheeks (mucosa)</td>
<td>3.7</td>
<td>0.1</td>
<td>1</td>
</tr>
<tr>
<td>Scalp</td>
<td>2.2</td>
<td>0.2</td>
<td>2</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>1.2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>1</td>
<td>1</td>
<td>15</td>
</tr>
</tbody>
</table>
### TABLE 3

**Telangiectasia: Sites, Incidence, and Density of lesions**

<table>
<thead>
<tr>
<th>Involved area</th>
<th>Percentage of patients showing involvement in each site</th>
<th>Distribution percentage per site of involvement (total 100%)</th>
<th>Mean no. lesions per involved area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>63</td>
<td>33</td>
<td>13</td>
</tr>
<tr>
<td>Mouth</td>
<td>48</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>Hands/wrists</td>
<td>37</td>
<td>41</td>
<td>34</td>
</tr>
<tr>
<td>Chest</td>
<td>8.3</td>
<td>2.4</td>
<td>6.2</td>
</tr>
<tr>
<td>Arms</td>
<td>4.3</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Legs</td>
<td>3</td>
<td>.5</td>
<td>3</td>
</tr>
<tr>
<td>Feet</td>
<td>2.7</td>
<td>0.8</td>
<td>5</td>
</tr>
<tr>
<td>Abdomen</td>
<td>2.7</td>
<td>0.4</td>
<td>2.7</td>
</tr>
<tr>
<td>Back</td>
<td>2.4</td>
<td>0.8</td>
<td>4.6</td>
</tr>
<tr>
<td>Neck</td>
<td>2.4</td>
<td>0.1</td>
<td>2</td>
</tr>
</tbody>
</table>

### TABLE 4

**Visceral Involvement: No. Cases and Type of Cases and Type of Lesion Based on 80/324 Patients**

<table>
<thead>
<tr>
<th>No. Cases*</th>
<th>Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>48</td>
<td>GI tract</td>
</tr>
<tr>
<td>27</td>
<td>Liver</td>
</tr>
<tr>
<td>15</td>
<td>Lungs</td>
</tr>
<tr>
<td>13</td>
<td>CNS</td>
</tr>
<tr>
<td>2</td>
<td>Urinary system</td>
</tr>
</tbody>
</table>

* Total of 105 due to cases with multi-organ involvement.
D. NEUROLOGIC COMPLICATIONS IN HHT

A study by Hodgson et al determined that neurologic complications have been observed in 8 to 12 percent of the members of families with HHT.²

Neurologic signs of HHT are reported at all ages, with peak incidence in the third to fourth decades, and result from pulmonary arteriovenous fistulas (60 percent), vascular malformation of the brain (28 percent) and spinal cord (8 percent), and portosystemic encephalopathy (3 percent).²

Neurologic complications of pulmonary arteriovenous fistulas are basically ischemic or septic in origin. Peripheral septic microemboli that avoid the pulmonary capillary filter by means of pulmonary arteriovenous fistulas may rest in the vasculature of the central nervous system, with ensuing bacterial meningitis, encephalitis, mycotic aneurysm, or abscess.²

Among 90 patients with HHT and documented central nervous system lesions, cerebral telangiectases were observed in 40 percent, cerebral arteriovenous malformations in 19 percent, and aneurysms in 7 percent.²

Meningeal and cerebral telangiectases in HHT patients have been associated with subarachnoid, intraventricular, and intracerebral hemorrhage; seizures; progressive hydrocephalus; cerebellar dysfunction; and visual loss. Cerebral arteriovenous malformations may cause generalized or focal seizures, headache,
intracranial bruit perceived by the patient or detected by the physician, transient sensory and motor deficits, subarachnoid hemorrhage, and ataxia.

**E. INVOLVEMENT OF INTERNAL ORGANS**

The age at the time of onset of symptoms fluctuated from 1 to 87 years. Thirteen percent of the patients were 30 years old or younger while 43% were 60 years old or older.19 This same study found that the frequency of visceral involvement increased with age until age 70 years and then decreased: between 60 and 70 years of age, there were 29 cases of visceral involvement (45%) in 64 patients, while between 70 and 80 years, in a group of 74 patients, there were only 10 cases (13.5%).19 Of 14 patients older than 80 years, only one patient had evidence of visceral involvement (7%).19 The author of this study offered no speculation as to why the occurrence of visceral lesions dropped off in frequency for the age groups 70 years and older. I found this very interesting, as one would expect signs and symptoms to become worse as one grows older.

GI signs and symptoms included hematemesis (vomiting of blood), rectal bleeding, and chronic anemia. Hepatic signs and symptoms were hepatomegaly (enlargement of the liver), cirrhosis (hardening of the liver), hepatic angioma (tumorous blood or lymph vessels of the liver), jaundice (syndrome characterized by hyperbilirubinemia and deposition of bile pigment in the skin and
mucous membranes with a resulting yellow appearance of the patient), ascitis (effusion of serous fluid into the abdominal cavity which causes inflammation), and hepatic murmur (a gentle blowing auscultatory sound coming from the liver).

Pulmonary signs and symptoms included PAVF (pulmonary arterio-venous fistula; an anomaly characterized by existence of a direct communication between the arterial and venous systems in the lung), thoracic murmurs (a gentle blowing auscultatory sound coming from the chest), cyanosis (bluish discoloration of skin and mucous membranes due to excessive concentration of reduced hemoglobin in the blood), dyspnea (difficult or labored breathing), clubbing of fingers, and hemoptysis (spitting up of blood).

Central nervous system (CNS) signs and symptoms were CNS involvement secondary to a PAVF (two cerebral abscesses and one coma due to air embolism), hemiplegia (paralysis of one side of the body), meningeal hemorrhage, cerebral hemorrhage, and telangiectatic lesions of spinal cord. Urinary system signs and symptoms included hematuria (discharge of blood in the urine).

**OCULAR MANIFESTATIONS**

**A. CONJUNCTIVAL INVOLVEMENT**

Brent, Schachat, and White's study reported that bleeding from the conjunctiva is uncommon and is limited to a few rare conditions. The paucity of reports seems to indicate that ocular
symptomatology in HHT is extremely rare. While HHT is a relatively rare disease, ocular involvement is common in these patients. A wide variety of ocular vascular lesions have been revealed in patients with HHT. In three studies, involvement of the eye was observed in 45% - 65% of patients, with the most common lesions being conjunctival telangiectases.  

According to McMahon and Maino, ocular involvement of HHT primarily involves the lids and palpebral conjunctiva. Small petechiae, spider vessels, and aneurysms are usually found when these structures are involved. The typical lesion starts as a dilatation of a bright red hue of the capillaries which later, as the venules become involved, changes to a violet or bluish color. In actuality, the mucous membrane lesions are bright red, whereas the skin lesions of the eyelid are more bluish in color. Vase and Vase report a pronounced similarity between conjunctival lesions and mucosal lesions associated with HHT elsewhere in the system. 

Possibly the first publicized case of conjunctival involvement was that of Gjessing who, in 1916, described a man, aged 52 years, who had three attacks of conjunctival hemorrhage prior to systemic bleedings. This same patient also had angiomas which involved the mouth and face.  

Mention was made in 1959 that a patient was seen in Dr. Jessop's clinic, in 1895, who was in a state of collapse from hemorrhage of an ulcerated nevus of the conjunctiva. By the late 1950's, there were only three other recorded cases of conjunctival involvement with HHT.
The first case of HHT with associated conjunctival telangiectases was disclosed in 1907.17 By the early 1950's, eleven cases involving the palpebral conjunctiva (Figure 11) had been described: Weber (1907); Nones, five cases (1909); Schwartz (1925); Schoen (1930); Stock, two cases (1944); and Reed (1948).17 Brant et al stated that many cases were not published in the ophthalmic literature and often consisted only of incidental mentions of conjunctival lesions, with no information as to whether they were complicated by hemorrhage.20 Brant also added that it was doubtful that all patients were examined by an ophthalmologist.20

Figure 1122

Typical conjunctival lesions in Osler's disease with clusters of telangiectases.
In one study, a group of 20 patients with documented HHT was examined. The diagnosis of HHT was based on family history, epistaxis, and cutaneous telangiectases. In this study, conjunctival telangiectases were noted in seven of the 20 patients (35%). These lesions were located on both the inferior and superior palpebral conjunctiva (Figures 12, 13, & 14) but none were seen on the bulbar conjunctiva.

Figure 12

(Miles). Under the upper lid of the left eye were several large spots.

Figure 13

(Miles). Similar spots were present on the conjunctiva of the right eye.

Figure 14

—Telangiectatic lesion in conjunctiva of right lower lid near lid border.
In another study, conjunctival lesions were observed in 20 of 47 patients with HHT (Table 6), with the conjunctival lesions equally distributed in localization between the upper and lower eyelid. No difference could be demonstrated between the two eyes. Affection of the conjunctival bulbi was only seen in one case. Although the lesions in this patient were bilateral they did not differ from the palpebral telangiectases.

**TABLE 6**

<table>
<thead>
<tr>
<th>Localization</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpebral Conjunctiva</td>
<td>19</td>
</tr>
<tr>
<td>Bulbar Conjunctiva</td>
<td>1</td>
</tr>
<tr>
<td>Retina</td>
<td>1</td>
</tr>
</tbody>
</table>

One study examined 29 members of an HHT - suspected family of four generations and found R-O-W disease in 11 of them. Of these 11, seven of the affected persons had conjunctival telangiectases.

Pandolfi and Ehinger compiled a case report study of a patient with conjunctival bleeding from HHT with an associated platelet dysfunction. A 72-year-old woman was admitted to a hospital as an emergency due to profuse, sudden, spontaneous bleeding from the right eye. The hemorrhage was stopped by use of a compression bandage, but started again as soon as the bandage was removed. The bleeding originated from the inferior conjunctival fornix. R-O-W disease was diagnosed on the basis of widespread telangiectases of
the skin and mucous membranes. The manifestation of the
telangiectases was characteristic of R-O-W disease (round and flat,
red to purple in color with a diameter of 1-3 mm). These changes
had a distribution which involved the mucosa of the lips and tongue,
the skin of the face and limbs, and the conjunctiva of the fellow eye.
Though treated with fibrinolytic inhibitors (tranexamic acid orally,
3g/day) and a compression bandage, it was not until two days later
that the bleeding was controlled by means of ligation of a cluster of
vessels in the lower palpebral conjunctiva. The results of lab tests
were normal except for those related to platelet function. The
bleeding time which normally ranges 8-12 minutes before stopping
was found, in this patient to be abnormally long (18 minutes).

The association of a defective platelet function, with the
vascular abnormality of R-O-W disease, seems to considerably
increase the risk and seriousness of bleeding. Also, the possible
coexistence of a qualitative platelet defect should be considered in
the examination of patients with HHT. Substances that reduce
platelet function such as aspirin, indomethacin, and dextrans are
contraindicated in those patients that have blood coagulation
problems.

From the previous case, the question arises as to whether HHT
patients have any other abnormal blood tests. In a study by Vase and
Grove, 26 of the 28 patients with HHT demonstrated anemia. The
median hemoglobin value was 5.5 mmol/L (range 2.9-8.7). Normal
values for men are 8.0-11.0, and for women, 7.0-10.0.
B. RETINAL INVOLVEMENT

Involvement of the retina in HHT is rare. In 1971, Davis and Smith estimated the occurrence of intraocular involvement to be less than 1% when based on 1500 cases of reported HHT.

From a review of the literature and of the reported cases the retinal changes seen with Rendu-Osler-Weber disease could be considered as specific or nonspecific, and coincidental. According to Davis and Smith, specific intraocular signs include: (1) tortuosity and segmental dilatations of retinal veins (Figure 15 & 15a); (2) hemorrhages of the retina; (3) neovascularization of the retina and optic papilla; (4) telangiectases of retinal vessels (Figures 16 & 17); and (5) hemorrhages of the vitreous.

**Figure 15**

- Typical retinal venous telangiectasis contrasted by photocoagulation. Note segmental venous dilatation, perivascular sheathing, and small punctate retinal hemorrhages.

**Figure 15a**

- Perivenous hemorrhages along superior temporal vessels following photocoagulation, OD.
Massa et al described an anemic appearance of the fundus, choroidal ruptures, and colloid degeneration of the retina as manifestations of this disease. However, it is likely that these signs, as well as retinitis pigmentosa, retinal detachment, cataract, and choroidal melanoma are coincidental findings.

Brant et al state that review of the following reported cases of intraocular involvement in HHT raises the question of whether these reports actually reflect manifestations of HHT, or if these findings are associated with a different disease process or are simply reports of nonspecific findings.
The first account of retinal lesions in R-O-W disease was by Francois in 1938. The patient, a hypertensive (BP 290/120) 74-year-old woman, presented with hypertensive changes in the right eye, tortuous arterioles with perivascular exudates, large swollen veins, retinal hemorrhages, an inferior retinal detachment, and ectatic veins on the optic nerve. Francois stated these changes in the retina could be confused with hypertensive retinopathy and recommended examination of other cases.

Although Gjessing, in 1916, characterized hemorrhagic retinopathy in a patient with HHT, no remark was made of retinal vascular disease. Other diagnoses are possible.

Landau, Davis, and Nelken scrutinized 29 members of a four-generation family with HHT, and found two sisters with retinal varices. These findings could represent a change related to the diagnosis of HHT, but vascular tortuosity is a common finding in healthy patients and need not signify a true association.20

In 1957, Roubin reported a case of newly-formed vessels on the optic disc in a patient with HHT.

In one study, in 1958, 15 patients with HHT were observed and one was found with retinal involvement and anemia. In this patient, there were retinal hemorrhages, which disappeared after treatment of the anemia by blood transfusions. According to Brent et al the retinal abnormality in this patient was more likely attributable to the anemia than directly to hereditary hemorrhagic telangiectasia.20

Brent, Schachat, and White state it is possible that one particular case of HHT of a 45-year-old white woman, that was reported by Davis and Smith in 1971, really had some other
obliterative vasculitis, Eale's disease, or simply multiple old branch retinal vein occlusion.\textsuperscript{20}

Some cases probably do correctly depict ocular abnormalities that are a result of the disease process in HHT.

Forker and Bean presented a case report of a 19-year-old boy with HHT who presented to a medical outpatient clinic of the University Hospitals on March 19, 1962, due to frequent nosebleeds which were first reported at the age of six. Upon ocular examination, a lesion was found in the left retina. About one disc diameter from the nerve head, a tangle of small vessels surrounded the inferior temporal branch of the retinal artery and its companion vein. The apparently normal part of the vein between the lesion and the optic disc was half the diameter of the vein peripheral to this area. The tortuous mass of vessels looked like a complex arteriovenous aneurysm, but no sign of venous pulsation was found. Ophthalmodynamometry revealed no increase in local venous pressure. The case history suggested no injury and no hint of spontaneous retinal bleeding in the past. The visual acuity was normal.

The mechanism by which an arteriovenous fistula in the retinal vascular system might occur in HHT is no more understood than is the mechanism for the cause of pulmonary arteriovenous fistulas in HHT.\textsuperscript{14} It is speculated that a vascular weakness caused rupture of the small vessels which led to a hematoma, enclosing an adjacent artery and a vein. During the process of resolution, a common channel was produced between the artery and vein. Although there was no suggestion of intracranial disease in this patient, the
appearance of the retinal arteriovenous communication was comparable to that of the von Hippel-Lindau syndrome. Von Hippel-Lindau, or angiomatosis of the retina, is a disease characterized by the immense dilatation and tortuosity of some retinal vessels and the development of angiomas, usually in the peripheral retina. This disease can be found in all ages, from early childhood to middle life, but tends to show more frequently during the third decade of life.

In 1968, Meyer-Schwickerath and von Barsewisch described the occurrence of a retinal telangiectasis in a patient with HHT that was supported by fundus photography.

Vase and Vase examined 47 patients with HHT in Denmark and discovered one case with a retinal abnormality. A clear arteriovenous malformation (a shunt between an upper temporal venule and artery) in the retina was found in this patient and was well documented by fluorescein angiography (Figure 18).

Figure 18

Fluorescein angiogram showing an arterio-venous shunt between retinal artery and upper temporal venule in the right eye of a 67-year-old woman with Osler's disease.
The retinal lesions seen in patients with HHT are usually stable and seldom cause symptoms. Treatment is rarely required.\textsuperscript{20}

**C. CASE OF HERPETIC KERATOUVEITIS ASSOCIATED WITH HHT**

McMahon and Maino authored a case report of a 50-year-old white male with a past history of ethanol abuse, who reported to the Kansas City V.A. Eye Clinic complaining of an acute decrease in vision of his left eye with photophobia and irritation of about 24 hours duration.\textsuperscript{21} In 1968, he had been diagnosed as having HHT, and reported numerous occurrences of epistaxis since childhood.\textsuperscript{21} Earlier medical checkups had revealed telangiectatic involvement of the oral and gastrointestinal mucosa, lungs, toes, fingers, and skin. Further medical history included cellulitis (leg), thrombophlebitis, mild right heart failure, microcytic anemia, chronic obstructive pulmonary disease, and ethanol abuse.

Autoamputation of a few fingers had occurred and is assumed to be due to ischemia instigated by arteriovenous malformations. The patient, in 1979, developed a marginal "melting macroulceration" of the left cornea that was thereafter successfully treated with antibiotics, topical steroids, and subconjunctival injections of heparin. It is believed that the ulcer was secondary to ischemia.\textsuperscript{21}

Ocular examination revealed visual acuities of 20/20 OD and 20/200 OS. The left eye presented with numerous corneal dendritic figures, vascularization, and inferior corneal thinning with stromal
haze. Cells and flare (both grade +2) were found in the anterior chamber and the vitreous was hazy. The left retina appeared grossly within normal limits. The other eye was within normal limits. Inspection of the lids in both eyes revealed numerous spider-like dilated vessels, aneurysms, and red blotches. The lower left lid had a conspicuous vessel group on the inferior lid margin. The upper left lid had an extended, smooth, raised mass with cutaneous spider vessels.

A diagnosis of herpetic keratouveitis was made based on the corneal dendritic lesions. The debilitating effect of HHT and ethanol abuse furnished an excellent environment for the herpes virus. The patient was referred for ophthalmologic consultation and appropriate medical treatment. The presence of herpetic keratouveitis associated with HHT had not been previously reported in the literature.21

D. CASE REPORT OF RUBEOSIS-GLAUCOMA AND HHT

History of the patient: At the age of 7, a male patient sustained a sudden loss of vision in his left eye. The patient denied any particular preceding illnesses or systemic diseases. The patient's parents also denied any systemic diseases. The older brother of the patient had extensive capillary malformations, but no eye involvement.

Examination revealed an extensive vitreous hemorrhage of the left eye which made inspection of the retina impossible. The right
eye exhibited a marked sclerosis of the retinal vessels. Approxima-
ty one month later, the left fundus was visible as the vitreous hemorrhage partially resolved. The retinal vessels appeared rather thin and some vessels seemed to grow into the vitreous. The vitreal hemorrhage never did completely disappear. Over a period of approximately 3 years, a cataract, rubeosis of the iris, and secondary glaucoma developed. The left eye became painful and blind. Six months later, it was enucleated when the patient reached 11 years of age.

In the right eye, similar vascular changes also developed. Treatment by photocoagulation was attempted twice, primarily because of vascular proliferations next to the optic nerve. This led to some improvement (a slowing of the progression of neovascularization), but the newly-formed capillaries in the retina never completely disappeared. Three years later the fundus was virtually unchanged. Visual acuity was severely reduced, most likely due to a cataract of the posterior lens capsule. For years the patient had impaired lung function and was constantly cyanotic. Chest x-rays showed evidence of numerous capillary and arteriovenous malformations with telangiectases and anastomoses. Tests indicated very low oxygen saturation in the aorta (81%) and a right-to-left anastomosis in the lung. Because of the extensive dilatations and anastomoses of the pulmonary capillaries, the diagnosis of R-O-W disease was made.23

None of the eyes with R-O-W disease had been examined histologically before. Blodi, Ririe, and Riekhof had the opportunity to conduct the first histological examination on the enucleated eye
of this 11-year-old patient with HHT, glaucoma, and rubeosis.

Macroscopically, the eye was of normal size. The retina was found thickened after a horizontal cross-section was made. The cornea appeared normal.23 There were numerous peripheral synechiae that occluded the angle of the anterior chamber. Newly-formed capillaries had covered the iris. Through contraction, these capillaries had formed an ectropium uveae. The epithelium of the lens had grown toward the posterior pole of the lens. The peripheral retina was atrophic. Several retinal vessels had grown through the internal limiting membrane of the retina, causing the hemorrhages into the vitreous. A portion of the retina was lifted up and away from the optic disk, and a dense membrane extended into the vitreous. This membrane was composed of connective tissue, glia, blood vessels, and macrophages containing blood pigment.

The main findings were newly-formed vessels within and in front of the retina. It was uncertain whether this was a primary malformation of the retinal vessels, the same as found in R-O-W disease in the skin and mucous membranes, or whether it was a secondary reactive proliferation due to the chronic lack of oxygen in the arterial blood.23 Blodi et al believe it is the latter because this would also explain the rubeosis of the iris and the secondary glaucoma.23

E. CASE REPORT OF FILAMENTARY KERATITIS ASSOCIATED WITH HHT

In 1968, Wolper and Laibson submitted an R-O-W disease case report study of a 31-year-old white man, who had had frequent bouts
of epistaxis for the past 20 years. These were, at times, spontaneous but more often were facilitated by very minor stress, e.g. nose-blowing. During the past 10 years, he had frequently noted a foreign body sensation in the eyes and on at least two occurrences, had bleeding from the eye after rubbing the eyelids (Table 7). Unlike the oral bleeding and epistaxis which the patient had commonly been able to stop by a few minutes of local self-applied pressure, his first recorded episode of bleeding from the eye (upper right lid, March 1963) was more prolonged and required consultation with an ophthalmologist. Thermal cautery was used to treat two ulcers on the upper eyelid. Although the foreign body sensation repeated itself frequently in both eyes, there was no recurrence of "bloody tears" until July 1966, when bleeding began after rubbing the lids. On this occasion, the bleeding appeared from the left upper lid and was arrested by a few minutes of localized pressure.

**TABLE 7**

**Ocular Symptoms and Objective Findings in Both Eyes From July 16, 1966 to June 16, 1968.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Right Eye</th>
<th></th>
<th>Left Eye</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Symptoms</td>
<td>Findings</td>
<td>Symptoms</td>
<td>Findings</td>
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<td>None</td>
<td>FBS</td>
<td>Filaments</td>
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<tr>
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<td>None</td>
<td>Upper left lid bled</td>
<td>Filaments</td>
</tr>
<tr>
<td>4-22-67</td>
<td>FBS *</td>
<td>Filaments</td>
<td>FBS</td>
<td>Filaments</td>
</tr>
<tr>
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<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
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</tr>
<tr>
<td>6-2-68</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>SPK</td>
</tr>
</tbody>
</table>

* Foreign body sensation
The most recent hemorrhage of the eye (July 20, 1966) occurred from the left upper eyelid after rubbing it. The patient managed to stop the bleeding in a few minutes by applying local pressure. After this episode, the foreign body sensation in the left
eye became more acute. When he was seen again two days later, one of the telangiectatic foci in the palpebral conjunctiva of the left upper lid appeared markedly congested with numerous petechial hemorrhages surrounding it.

Corneal filaments with punctate fluorescein staining of the corneal epithelium were noted intermittently (Table 7). There was mild injection of the adjacent limbal conjunctiva when the filaments were present, but there had been no papillary hypertrophy, no proliferation of limbal tissue in the injected areas, and no staining of the bulbar conjunctiva when rose bengal or fluorescein were applied. The Schirmer test was normal, and corneal sensation had been intact and equal in both eyes when tested with the Cochet-Bonnet aesthesiometer.

The sporadic appearance of filamentary keratitis in this case report is an interesting finding (Table 7). Although the telangiectases on the conjunctiva were constant in location, the punctate keratitis and filaments were not always present and their location varied. Treatment for the filamentary keratitis included antibiotics and corticosteroids when it was believed that a low-grade staph infection might have precipitated the keratitis. On one occurrence, lid massage and 1% silver nitrate applied to the lid margins may have hastened the departure of the filaments. It appeared, however, that the filaments and punctate keratitis occurred and resolved with inconsistency. The presence of filaments in both eyes (Aug. 30, 1967) and the complete absence of symptoms during this one particular visit may be an indication of the variability of these filaments and the reaction they induced.
If there is an association between HHT and the keratitis in this patient, several theories are suggested. If a local process is involved, perhaps it is a physiological interference with maintenance of the normal precorneal tear film by the dilated thin-walled telangiectases absorbing constituents from its liquid or mucoid layers. This hypothesis is unlikely due to the inconsistent presence of the filaments. The commonly-found chalazion which usually presents on the palpebral conjunctiva of an individual does not typically grossly disturb the cornea. So, one should ask how the telangiectases could cause the keratitis. Perhaps, in this case, the secretions of one or more of the various lacrimal glands which contribute to the precorneal tear film are abnormal. When the patient was last examined, there were no dry spots observed in the precorneal tear film of either eye.

E. DIFFERENTIAL DIAGNOSIS

To make a diagnosis of HHT, the three postulates of Hanes, Larrabee, and Littman must be considered: (1) a history of heredity; (2) visible telangiectases distinctly pathologic in numbers and distribution; and (3) a tendency to bleed from the lesion. The condition of HHT need not be confused with other hemorrhagic conditions, because, significantly, there is no abnormality in the blood picture other than that associated with secondary anemia. The bleeding and clotting times and the platelet count are all normal.
The disease is clearly nonhemophilic and nonpurpuric. Differential diagnosis should include hemorrhages observed in cirrhosis of the liver; leukemia; and Hodgkins, Gaucher, and Banti diseases. The telangiectases that occasionally show in lead poisoning, pregnancy, and senility should also be considered. A relationship to von Hippel-Lindau, Sturge-Weber, and Bourneville diseases has also been postulated.7

There are a number of local and systemic diseases that produce vascular changes in the conjunctiva. A listing by Duke-Elder of conditions in which hemorrhage from the conjunctiva can be seen includes:

1. HHT
2. Vicarious menstruation
3. Hemophilia
4. Conjunctivitis
5. Hysteria
6. Jaundice
7. Vascular tumors
8. Granulomas
9. Advanced atheromas
10. Post-silver nitrate therapy
11. Regurgitant flow of blood through the nasolacrimal duct
12. Strenuous effort in normal individuals20

Among the many diseases in which telangiectases may manifest; only two will be discussed. CRST syndrome, characterized by subcutaneous calcinosis, Raynaud's phenomenon, sclerodactyly, and multiple telangiectases, is a benign nonprogressive form of
scleroderma. The macroscopic appearance and distribution of the vascular lesions is identical to those of HHT. CRST syndrome is distinguished by a decreased frequency of hemorrhage, predominance of females affected (HHT affects both sexes equally), and later appearance of the vascular changes.

In ataxia telangiectasia (Louis-Bar syndrome), telangiectases are found on the face, ears, and conjunctiva: A familial pattern exists. In HHT, occasional cases have been found with vascular lesions on the bulbar conjunctiva. In ataxia telangiectasia, these lesions are typically bulbar in distribution, and the overall clinical picture is unique, presenting no problem in differential diagnosis.

There are many differential diagnoses of intraocular lesions seen in HHT. A small arteriovenous malformation (Figure 20) is the typical vascular lesion. In HHT, hemorrhage and lipid are absent, and the angiogram fails to demonstrate nonperfusion or leakage. When some of the ocular features of HHT (i.e. telangiectases) are present, the following differential diagnoses should be considered:

1. Hypertensive retinopathy
2. Branch retinal vein occlusion
3. Diabetic retinopathy
4. Coat's disease
5. Eale's disease
6. Vascular changes seen in ataxia telangiectasia
7. Phakomatoses
There have been a number of reports of fundus irregularities in patients with HHT, such as retinal vessel tortuosity and dilatation. However, this is common and may be seen in normal patients as well as in other disease processes. Retinal and disk neovascularization is another fundus abnormality found in HHT patients, normal patients, and in other disease processes. When these manifestations are discovered in a patient with HHT, the practitioner may be mistakenly led to believe that these are unique signs of HHT. In reality, these signs and symptoms experienced by a patient with HHT may be due to an entirely different disease or syndrome. When patients have signs and symptoms of two or more different disease processes, the diagnosis becomes quite challenging and sometimes
impossible. In order to make the proper diagnosis of HHT we are reminded again of the three postulates of Hanes, Larrabee, and Littman: (1) a history of heredity; (2) visible telangiectases distinctly pathologic in numbers; (3) a tendency to bleed from the lesion.7

F. TREATMENT

In general, treatment has been a disappointment, and the backbone of all therapy is still blood transfusions and tamponage.7 Radiologists and dermatologists shy away from radiation therapy because the multiple lesions expose the patient to an undesirable accumulative dosage, and because eradication of a lesion usually results in formation of a nearby satellite lesion.7

By 1955, Garner and Grossman reported that the multiplicity of therapeutic measures found in the literature, coupled with the paucity of uniformly good or even fairly good results, was indicative of the inadequacy of the measures available to combat HHT.7 To date, no specific agent to treat HHT has been found.

Since the most frequent presenting complaint of this disease is epistaxis, it is not surprising to find the literature packed with therapy directed toward nasal surgery.

Chromic-acid chemical cauterization was successfully reported by Houser for three of his cases. A fourth case presented with satellite lesions in the immediate vicinity of the chemically-treated and destroyed lesions. Within a very short period of time,
these new lesions appeared and showed the same tendency to hemorrhage as the preceding lesions. These satellite lesions developed adjacent to the recently destroyed angiomatous lesions, irrespective of the manner in which they had been destroyed. It was suggested that this form of destructive trauma may be enough to stimulate the formation of new angiomas, thus indicating a neoplastic rather than angiectatic origin of these vascular lesions. On occasion, perforation of the nasal septum would be observed following chromic-acid cauterization but Houser believed this was preferable to nosebleeds.

Molesworth advised early radiation of nasal lesions, regardless of location. However, Houser found poor results from radium, x-rays, or electrocoagulation, and favored chemical cauterization as mentioned. Radium was utilized, with success, by Scal and Sterman, while Weiss described only temporary results and preferred the use of snake venom. Many authors used radium as the treatment of choice; whereas others believed that radium produced greater tissue friability and subsequent bleeding, and therefore censured its use.

Peluse employed vitamin K, vitamin C, and bile salts without any appreciable effect. Peluse also used sylnasol, a sclerosing and fibrous-tissue proliferating agent with no enthusiastic results, except that good results were found with the use of vitamin P. However, Shapiro perceived vitamin P as worthless.

Cipollaro successfully employed electrolysis, using the negative pole of a galvanic current as the active electrode and
enlisting multiple punctures, the number dependent on the size of
the lesion.

Peck and Rosenthal used moccasin snake venom in 1935 and
had good results in the control of bleeding. This was matched by
Ingalls and Weiss. Figi and Watkins, on the other hand, of the Mayo
Clinic, revealed poor results from this form of therapy.

Koch, Esher, and Lewis successfully employed hormonal
therapy. This therapy was based upon the fact that exacerbations of
epistaxis were noted during periods of reduced estrogen secretion,
premenstrually and following x-ray castrations. In male patients, it
was necessary to add methyl testosterone in order to nullify
feminizing features that developed. In a very thorough and
comprehensive report, Dolowitz observed that of all the suggested
therapeutic regimes none, including the most recent hormones, was
effective.

Once significant epistaxis has begun, local nonspecific therapy
is not only ineffective but frequently enhances bleeding. Destroying
septal mucosa or producing scar tissue may reduce the chance of
future control. Two forms of therapy have been shown to achieve
prolonged remission of epistaxis: oral estrogen and septal
dermoplasty. Although topical estrogens do not seem to have a
lasting effect, oral estrogens may decrease epistaxis in HHT.
According to many, the most successful definitive operative
procedure is the septal dermoplasty. In this procedure, the
pathologic mucosa is removed from the septum and turbinates, and
replaced by a split skin graft. The idea of replacing the anomalous
mucosal lining with split skin has proven itself valuable in reducing
bouts of epistaxis in most patients. Septal dermoplasty has been reported to reduce the frequency and severity of epistaxis in up to 75 percent of patients for months or years.

The best candidates for septal dermoplasty are those with disabling epistaxis from telangiectatic lesions mostly on the anterior nasal mucosa. Success of this surgical procedure is dependent on adequately grafting the mucosa of the anterior nasal septum and floor with a protective covering of skin. However, dermoplasty is not guaranteed to stop all symptoms. Failure of this procedure is ascribed to not enough graft coverage, subsequent graft shrinkage that re-exposes mucosa, or bleeding from lesions beyond the borders of the graft.

G. OPTOMETRIC MANAGEMENT OF HHT

The optometric management of HHT includes identifying ocular adnexa telangiectases, conjunctival telangiectases, and suspicious retinal lesions.

The following management guidelines are offered to suit individual needs in every case because the severity of the disease is so variable.

The eye care practitioner should carefully examine the nasal septum, oral mucosa, and skin of the neck and face in patients with retinal and/or conjunctival telangiectases, and should inquire about a family history of epistaxis or a bleeding diathesis. There are no references concerning treatment of the conjunctival aspects of the
The primary eye care practitioner should keep in mind any possible local and systemic diseases or conditions that can cause hemorrhaging of the conjunctiva. Those that mimic the conjunctival bleeding of HHT include vicarious menstruation, hemophilia, conjunctivitis, hysteria, jaundice, vascular tumors, granulomas, advanced atheromases, post-silver nitrate therapy, regurgitant flow of blood through the nasolacrimal duct, and in normal individuals it can be associated with strenuous effort. For retinal lesions, the eye care practitioner should consider ruling out several other diseases in order to differentially diagnose those retinal lesions caused by HHT. When intraocular features (i.e. retinal telangiectasis) is present the following differential diagnoses should be considered by the eye care practitioner: hypertensive retinopathy, branch retinal vein occlusion, diabetic retinopathy, Coats disease (exudative retinopathy), Eale's disease (a condition with recurrent hemorrhaging in the retina and vitreous), the vascular changes seen in ataxia telangiectasia, and the phakomatoses. Those patients with retinal lesions should be referred to a retinal specialist. In general, retinal lesions seen in patients with HHT are stable, seldom cause symptoms, and treatment is rarely required.

Persons with abundant dermal vascular spiders and a history of repeated nose bleeds or coughing up blood should be referred to an internist for supplementary evaluation.

Patients seeking genetic counseling concerning HHT should be advised of the natural history and consequences of the condition. Mention should be made by the eye care practitioner to those HHT patients whose occupations or hobbies involve heavy lifting or
strenuous exercise that these activities should be avoided because they tend to put an excess pressure on the walls of the vessels of the vascular system and could eventually lead to a heightened severity of aneurysmal formations in any organ of the body, including the brain.

SUMMARY AND CONCLUSION

Hereditary hemorrhagic telangiectasia is an autosomal dominant disorder characterized by telangiectases, and sometimes arteriovenous malformations and aneurysms throughout various vascular beds in the body.

Some facts about HHT include the following:
1. affects both sexes equally
2. more common in the European population
3. manifestations become milder in successive generations
4. there is a higher incidence of blood group 0 as compared to the background population
5. homozygotes may not survive more than a few months
6. epistaxis is the most frequent complaint and systemic manifestation

The lesions may be nonexistent or not visible in early life, but become apparent between the third and fourth decade. The vascular abnormalities are described pathologically as thin endothelial tubes arranged in spider-like or stellate patterns that are prone to multiple and frequent hemorrhage. The tendency to bleed is more
pronounced after the third or fourth decade and is responsible for the epistaxis, anemia, and low blood volumes found commonly among these patients. Death from internal bleeding of telangiectases is rare, but possible.

Ocular involvement principally involves the palpebral conjunctiva and lids. Spider vessels, small petechia, and aneurysms are commonly found. Involvement of the retina is very rare, with only a few reported cases of intraocular involvement.

Signs and symptoms of HHT can be differentially diagnosed from other similar diseases based on the three postulates of Hanes and Larrabee and Littman.

To this day, no specific treatment has been found that will cure HHT. There have been many therapeutic measures attempted to solve the problem of severe epistaxis, but the most successful technique has been the surgical microvascular free flap technique. As in the past, the most common tools to combat hemorrhaging are direct pressure, oral iron supplementation, and for more severe cases blood transfusions.

The optometric management of a patient with newly-discovered HHT signs should include education of patient, regular follow-ups, and possible referral to a retinal specialist or internist. The patient who has already been apprised of his or her condition of HHT should be followed optometrically on a regular basis to monitor for any vascular changes that may occur in the retina, conjunctiva, or eye in general.

Review of the reported cases of intraocular involvement in HHT raise the question of which reports actually reflect
manifestations of HHT. The cases of HHT with arteriovenous malformations in the retina are widely viewed as true signs of HHT that manifest in the eye. It is also extensively accepted that telangiectatic lesions that occur in the palpebral conjunctiva are also characteristic of HHT. When literature is reviewed that deals with cases of HHT and signs of nevus in the conjunctiva, choroidal ruptures, vascular tortuosity in retina, or rubeosis-glaucoma one must ask whether these signs are specific, non-specific, or coincidental. Authors of the literature reviews of HHT differ widely in their opinions on what constitutes specific vs. coincidental. One author e.g. may believe that tortuous retinal vessels are a specific sign of HHT yet another author may hold the opposite opinion that they are found in normal individuals too.

Due to the paucity of literature, the rarity of the disease itself, and the difference of opinion on HHT signs this makes it truly necessary for the primary eye care practitioner to be well versed on the subject of hemorrhagic diseases that manifest in the eye. The complicated history of a patient with multiple problems encountered reaffirm the need for optometric awareness of rare diseases, so that responsible clinical decisions can be made.
REFERENCES


