Pediatric Retinal Vascular Diseases

From Angiography to Vitrectomy

Ulrich Spandau
Sang Jin Kim

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Ulrich Spandau
Ophthalmology
University of Uppsala Ophthalmology
Uppsala
Sweden

Sang Jin Kim
Department of Ophthalmology
Samsung Medical Center
Sungkyunkwan University
Seoul
South Korea

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Preface

Dear reader,
This book provides comprehensive and up-to-date information on diagnosis, medical, and surgical treatments for pediatric retinal vascular conditions, which are leading causes of childhood blindness throughout the world. Experienced ophthalmologists in this field discuss basic knowledge about these diseases, practical aspects of management such as exam under anesthesia, up-to-date diagnostic approaches including spectral-domain handheld optical coherence tomography (OCT), and OCT angiography. A high emphasis is placed on recent advances in medical and surgical treatments for pediatric retinal vascular diseases. Step-by-step instructions are given for the surgical treatment with anti-VEGF treatment, laser photocoagulation, and vitrectomy. Both the general ophthalmologist who cares for children with retinal diseases and the specialist (pediatric ophthalmologists and vitreoretinal surgeon) will find this book to be an informative resource in providing best care for children with pediatric retinal vascular conditions.

The book includes many videos, which demonstrate the surgeries step-by-step. All videos are listed in the Video list and can be accessed under http://extras.springer.com/Search. Enter the ISBN number of your book and download the videos.

Alternatively, the online version of every chapter contains the videos. Note the following footmark at the beginning of every chapter:

"**Electronic Supplementary Material** The online version of this chapter (https://doi.org/10.1007/978-3-030-13701-4_16) contains supplementary material, which is available to authorized users." Copy and paste the https address in your browser and you can access the videos.

Uppsala, Sweden — Ulrich Spandau
Seoul, South Korea — Sang Jin Kim

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I want to thank my family and especially my wife Katrin for her never-ending patience with a husband who spends so much time with his books.

Ulrich Spandau

Contents

Abbreviations

FA	fluorescein angiography
FEVR	familial exudative vitreoretinopathy
GA	gestational age
LE	left eye
LIO	laser indirect ophthalmoscopy
PHPV	persistent hyperplastic primary vitreous
PMA	postmenstrual age
RE	right eye
ROP	retinopathy of prematurity

List of Videos

The videos can be accessed under http://extras.springer.com/Search. Enter the ISBN number of your book and download the videos.

Video 16.1	Injection of Lucentis for ROP
Video 21.1	Insertion of trocars
Video 21.2	Vitrectomy for ROP stage 4B RE
Video 21.3	Vitrectomy for ROP stage 4A LE
Video 21.4	Bilateral vitrectomy for ROP stage 4A and 4B (long audio)
Video 21.5	ROP stage 4B (very short)
Video 22.1	Encircling band and ROP
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Video 24.1	Stage 4B with fibrovascular membranes
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Part I
Pediatric Retinal Diseases

Chapter 1
Coats Disease

1.1 Diagnosis of Coats Disease

1.1.1 Introduction

Coats disease is an idiopathic retinal vascular disorder characterized by retinal telangiectasia, exudation, and exudative retinal detachment. In 1908, George Coats first described case series with retinal telangiectasia and massive exudation [1]. Coats disease occurs most commonly in males in the first or second decades, but it can be diagnosed at any age. The majority of cases are unilateral, but recent studies using wide-field fluorescein angiography revealed that subclinical abnormalities such as peripheral nonperfusion are common in contralateral eyes [2, 3]. The clinical manifestations of Coats disease are highly variable, ranging from telangiectasia only to phthisis bulbi.

1.1.2 Pathogenesis

1.1.2.1 Histopathology

A histologic study on enucleated eyes with Coats disease revealed macrophage infiltration and cholesteric clefts in the subretinal space [4]. Retinal vascular abnormalities were also demonstrated including dilated vessels with hyalinized vessel walls [4]. Immunoreactivity for VEGF was observed in the detached retina, dilated vessel, and macrophages infiltrating the subretinal proliferative tissue [4]. VEGFR-2 immunoreactivity was also observed in endothelial cells located in abnormal retinal vessels and inner layer of the detached retina, but not in macrophages infiltrating the subretinal space [4].

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1.1.3 Genetics

Previous studies reported mutations in several genes including *NDP* [5], *CRB1* [6], *TINF2* [7], *PANK2* [8], and *ABCA4* [9] in patients with Coats disease or Coats-like retinal phenotype. However, the exact molecular mechanisms remain to be elucidated.

1.1.4 Clinical Characteristics

1.1.4.1 Fundus Findings [10–12]

Retinal vascular telangiectasis (Figs. 1.1 and 1.2) develop most commonly in the inferior and temporal quadrants between the equator and the ora serrata [12]. Affected vessels show irregular and aneurysmal dilations. Vascular leakage from

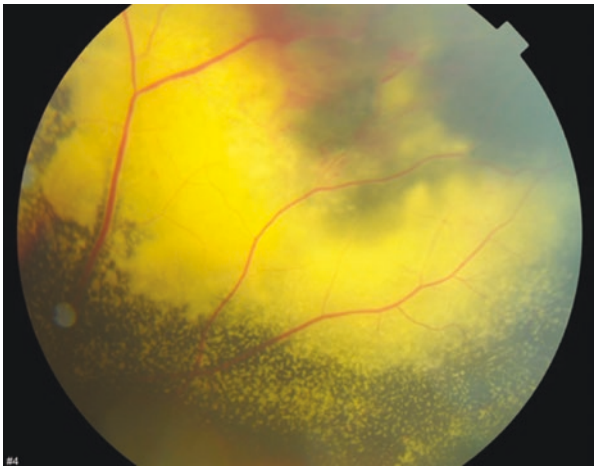

Fig. 1.1 Peripheral telangiectatic vessels with massive exudation and retinal detachment

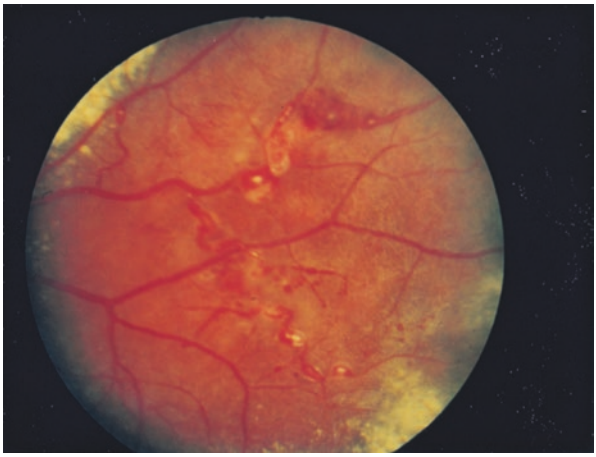

Fig. 1.2 Typical area of retinal telangiectasia without associated exudation. (Reprinted from Shields et al. [12]. Copyright (2001), with permission from Elsevier)

the abnormal vessels result in lipid-rich exudation (Figs. 1.3 and 1.4) and progressive fluid accumulation with subsequent serous retinal detachment (Figs. 1.5, 1.6, and 1.7) [11]. Macular edema or subretinal fluid is a common cause of visual symptom.

Retinal pigment epithelial cells that proliferate and migrate into the subretinal space may develop subretinal fibrous proliferation [11].

The vitreous usually remains clear [11]. Vitreoretinal traction, fibrosis, or proliferative vitreoretinopathy are not common but epiretinal membrane may develop [11].

In a large-scale case series (n = 150 patients) study by Shields et al. in 2001 [10], median age at the diagnosis was 5 years. Among the 150 patients, 114 (76%) were males and 142 (95%) showed unilateral involvement [10]. The most common referral diagnoses were Coats disease in 64 (41%) followed by retinoblastoma in 43 (27%) patients [10]. Visual acuity at presentation was 20/200 or worse in 121 eyes (76%) [10]. The retinal telangiectasia involved the midperipheral or peripheral

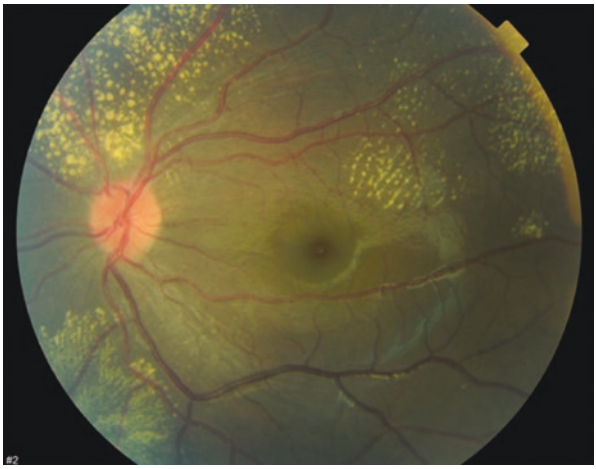

Fig. 1.3 Exudates at posterior pole in an 8-year old boy with Coats disease

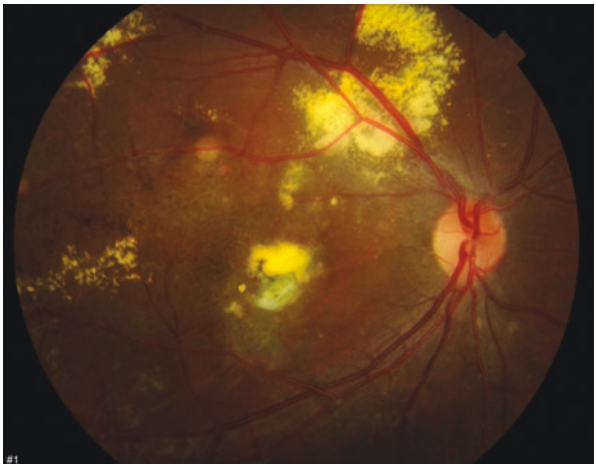

Fig. 1.4 Long-standing exudates at posterior pole in Coats disease

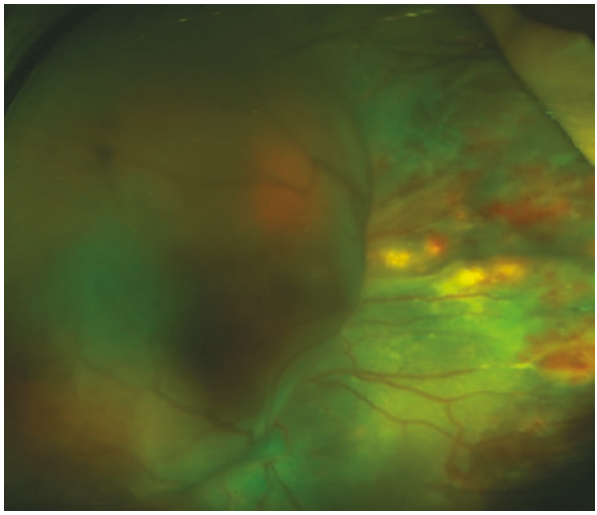

Fig. 1.5 Total retinal detachment in Coats disease

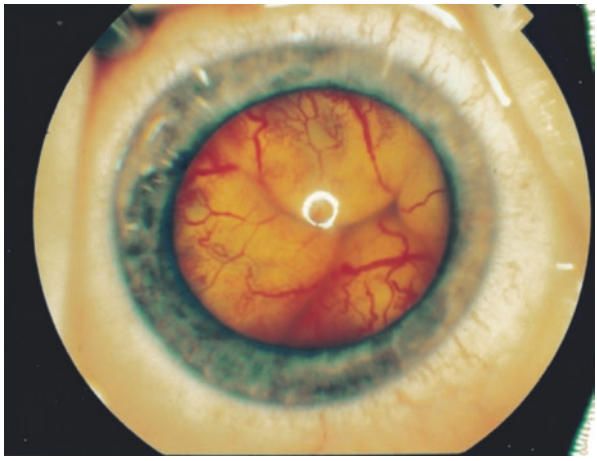

Fig. 1.6 Total retinal detachment in a patient with Coats disease. (Reprinted from Shields et al. [12]. Copyright (2001), with permission from Elsevier)

fundus in 98% of eyes [10]. Retinal exudation was present in six or more clock hours in 115 eyes (73%) [10]. Total retinal detachment was seen in 74 eyes (47%) and neovascular glaucoma in 12 eyes (8%) [10].

1.1.5 Fluorescein Angiography

Wide-field angiography systems such as RetCam (Natus) or Ultra-widefield™ retinal imaging systems (Optos) are essential in diagnosis and management of Coats disease. The angiographic features of Coats disease include areas of nonperfusion, peripheral telangiectatic capillaries and "light bulb" aneurysms, vascular leakage,

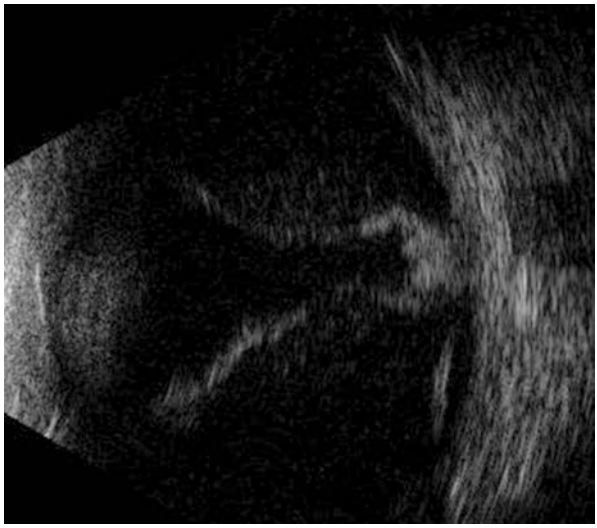

Fig. 1.7 B-scan ultrasonography of total retinal detachment in a 12-year-old boy

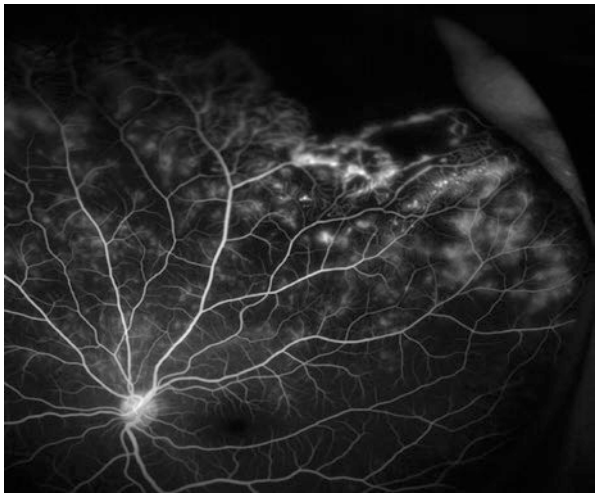

Fig. 1.8 Ultra-wide field fluorescein angiography showing dilated peripheral vessels with leakage in a patient with Coats disease

and blocked fluorescence from exudates (Figs. 1.8, 1.9, 1.10, and 1.11) [11]. Fluorescein angiography is essential in early detection of vascular abnormalities especially in eyes with telangiectasia only.

1.1.6 Optical Coherence Tomography (OCT)

In Coats disease, OCT is useful in identifying macular edema and subretinal fluid and to evaluate response to treatment. Subretinal fluid and exudate may be visible with OCT in patients with Coats disease (Figs. 1.12 and 1.13). It should be noted

Fig. 1.9 Ultra-wide field fluorescein angiography showing dilated peripheral vessels and nonperfusion in a patient with Coats disease

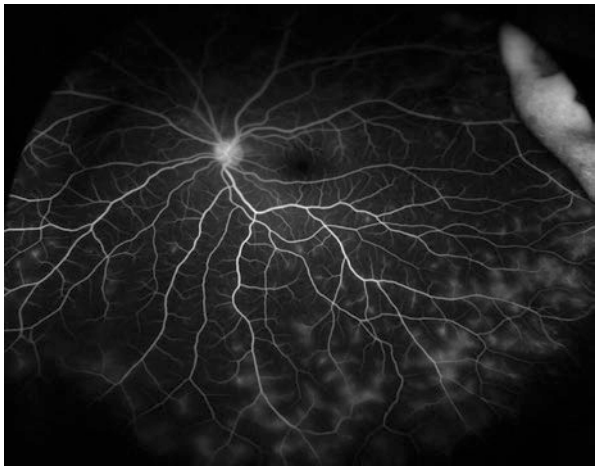

Fig. 1.10 Mild late leakage in normal-looking vessels in the inferior periphery in a patient with Coats disease

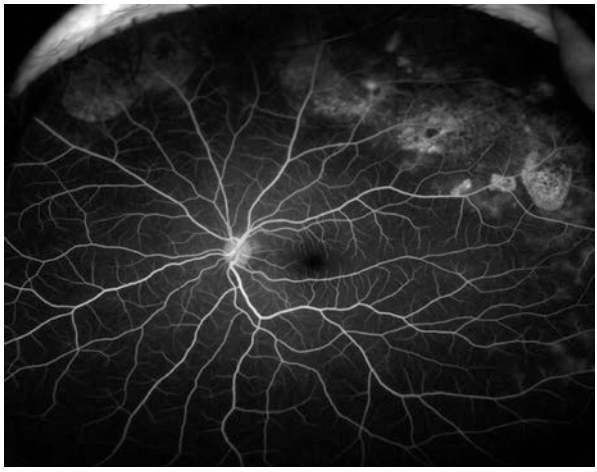

Fig. 1.11 Decreased leakage after cryotherapy in a patient with Coats disease

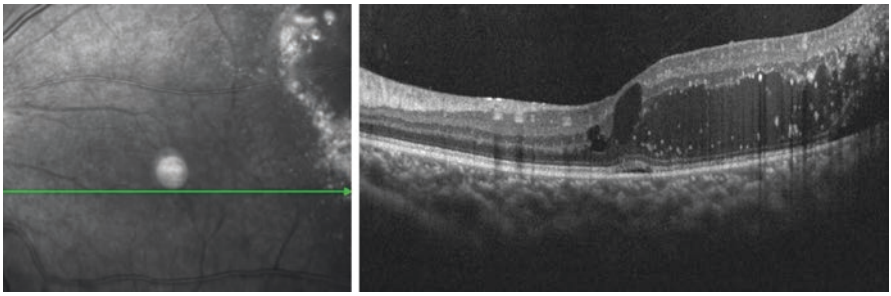

Fig. 1.12 SD-OCT showing macular edema and exudates in a patient with Coats disease

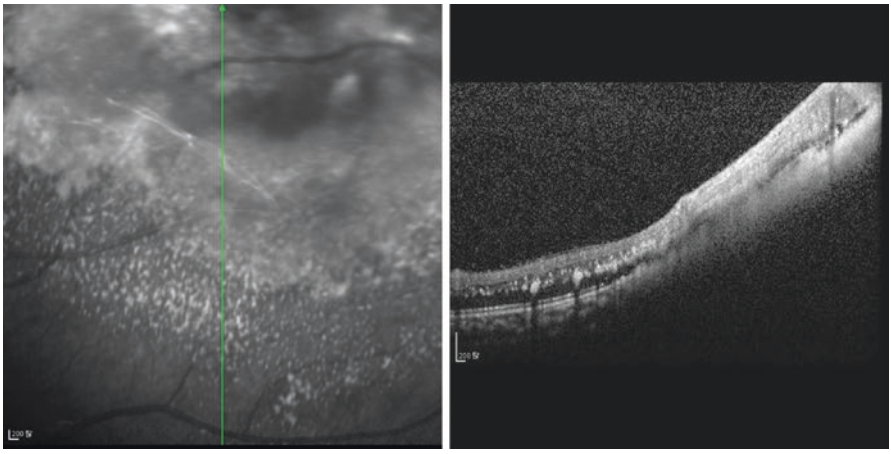

Fig. 1.13 SD-OCT showing intraretinal lipid deposits in a patient with Coats disease

that in eyes with large amount of subretinal fluid, the amount of subretinal fluid seen on OCT scans taken in a sitting position may be different from that in a supine position due to fluid shifting.

1.2 Classification of Coats Disease

1.2.1 A Classification System

Shields et al. proposed a classification system of Coats disease based on their clinical observations in 150 consecutive patients in 2001 [10]. Their proposed classification system is now being widely-used and very helpful for selecting treatment methods and predicting the visual outcomes (Table 1.1 and Fig. 1.14).

Table 1.1 Staging classification of Coats disease [10]

Stage	Findings
1	Retinal telangiectasia only
2	Telangiectasia and exudation
A	Extrafoveal exudation
B	Foveal exudation
3	Exudative retinal detachment
A	Subtotal detachment 1. Extrafoveal 2. Foveal
B	Total detachment
4	Total retinal detachment; glaucoma
5	Advanced end-stage disease

Eyes with stage 1 disease can be managed by either regular follow-up exams or laser photocoagulation [10]. In stage 1 disease, there is high probability that the eye can be salvaged and the visual prognosis is usually favorable [10]. However, stage 1 disease is rare in a real clinical practice probably due to no symptoms.

Eyes with stage 2 disease can be managed by laser photocoagulation or cryotherapy, depending on the extent and location of the disease [10]. In stage 2A, the visual prognosis is generally good [10]. Eyes with stage 2B are usually salvaged and the visual prognosis is fairly good [10]. Visual prognosis of eyes with a dense yellow gray nodule by the foveal exudation is usually worse [10].

Eyes with stage 3A disease can generally be managed by photocoagulation or cryotherapy [10]. Some of the patients with stage 3A1 disease (extrafoveal subtotal retinal detachment) in a sitting position can reveal subfoveal fluid in a supine position (thus stage 3A2). Even if the retinal detachment involves the fovea, it will resolve when the telangiectasias are treated [10]. Laser photocoagulation is less effective in areas of retinal detachment, and cryotherapy is often preferable in such instances [10]. However, Levinson and Hubbard reported good anatomical outcome of 577 nm yellow laser photocoagulation in 16 patients including 5 patients with stage 3B disease [13]. Patients with stage 3B with bullous detachment may require surgical treatment (e.g. external subretinal fluid drainage).

Patients who present with stage 4 disease are often best managed by enucleation to relieve the severe ocular pain [10]. Patients with stage 5 disease generally have a blind, but comfortable eye and require no aggressive treatment [10].

1.2.2 Stage and Visual Outcome

The staging system of Coats disease is helpful for selecting treatment and predicting the ocular and visual outcomes. In a case series study including 150 patients from 1975 to 1999, the visual outcome was generally poor [10]. The proportion of

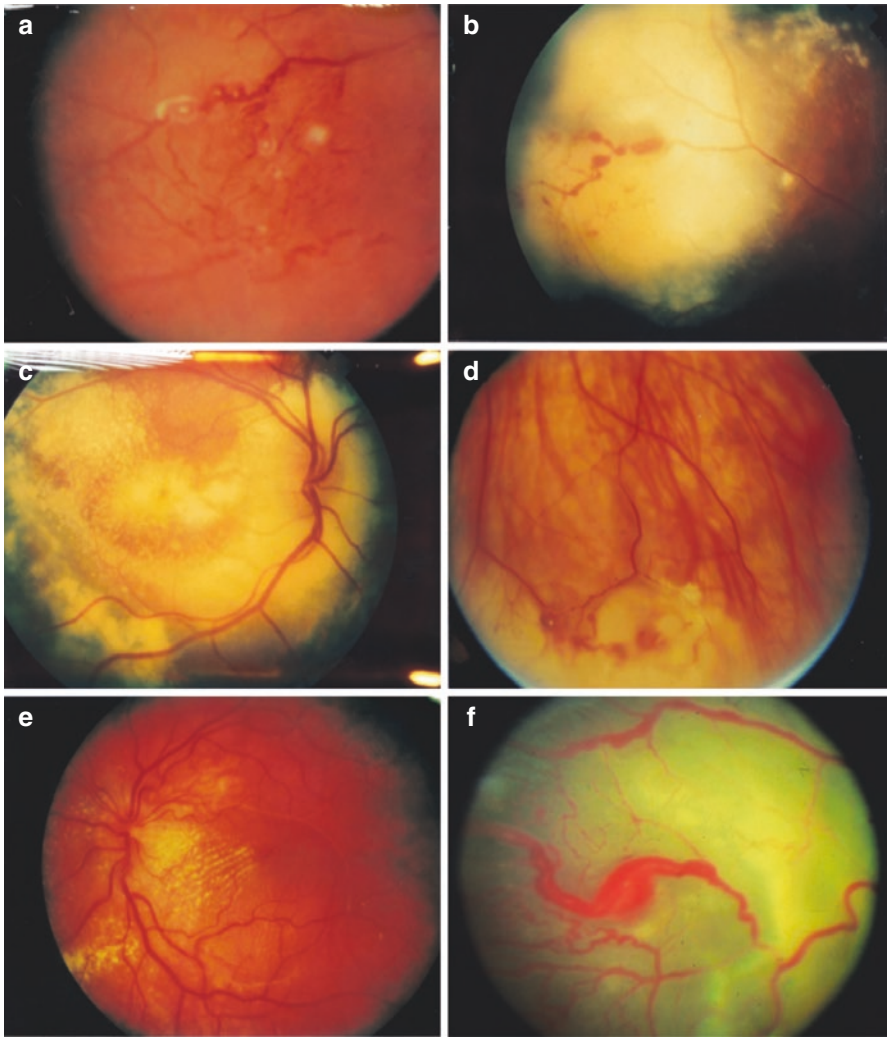

Fig. 1.14 Examples of stages of Coats disease. (**a**) Stage 1, retinal telangiectasia only. (**b**) Stage 2A, telangiectasia and extrafoveal exudation. (**c**) Stage 2B, foveal exudation. (**d**) Stage 3A1, subtotal retinal detachment inferiorly, sparing the fovea. (**e**) Stage 3A2, subtotal retinal detachment extending beneath the fovea. (**f**) Stage 3B, total exudative retinal detachment. (**g**) Stage 4, total exudative retinal detachment behind the lens in eye with secondary glaucoma. (**h**) Stage 5, advanced end stage disease with chronic inflammation, posterior synechia and cataract, secondary to longstanding retinal detachment. (Reprinted from Shields et al. [12]. Copyright (2001), with permission from Elsevier)

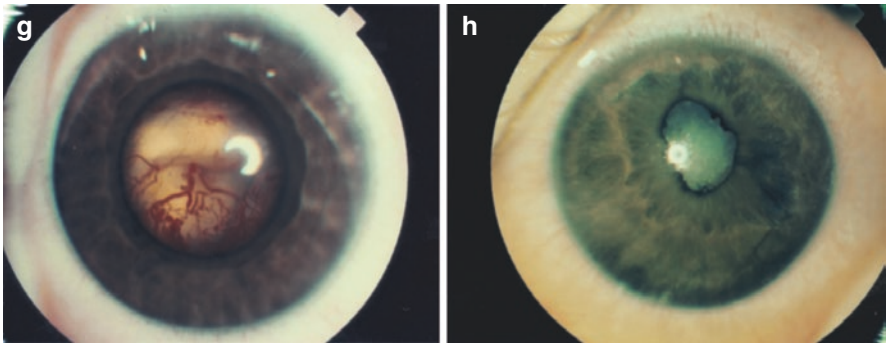

Fig. 1.14 (continued)

Table 1.2 Visual outcome according to the stage of Coats Disease

	Shields et al. [10]		Ong et al. [14]			
			1995–2005		2006–2015	
Stage	% poor visual outcome[a]	Number of eyes	% poor visual outcome[a]	Number of eyes	% poor visual outcome[a]	Number of eyes
1	0	1				
2A	30	10	50	2	0	1
2B	86	7	67	3	33	3
3A1	70	25	80	5	70	10
3A2	70	23				
3B	94	37	100	5	100	3
4	100	18	100	1		0
5	100	3		0		0

[a]Poor visual outcome was defined as BCVA of 20/200 or worse

poor visual outcome (20/200 or worse) was high in eyes with stage 2B through 5 (Table 1.2). Recently, Ong et al. [14] compared visual outcome between two time periods (decade 1, 1995–2005 and decade 2, 2006–2015), and showed that (1) there was a trend for the mean initial presenting VA for decade 1 eyes to be worse than for decade 2 eyes; (2) from initial to final follow-up visit, mean VA also worsened for decade 1 eyes, but remained stable for decade 2 eyes; (3) at the end of follow-up, there was a trend for mean VA for decade 1 eyes to be worse than for decade 2 eyes; and (4) decade 2 eyes had a higher average number of procedures per eye compared with decade 1 eyes (Table 1.2). In conclusion, this study showed that the earlier presentation of disease in decade 2 suggests improvements in disease detection over time, and there was a trend for eyes to have better final VA in decade 2.