# ACUTE RETINAL NECROSIS (ARN)

Eye Learn

All about the Eye

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# ACUTE RETINAL NECROSIS

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All about the Eye

1. Clinical signs and treatment of acute retinal necrosis. (2008)
2. A 30-year-old male presented with genital lesions and complained of sudden diminution of vision is one eye followed 6 weeks later by similar diminution in the other eye. What are the possible diagnoses? Give broad guidelines in the management of each situation. 2+8 D2015

**Introduction**- Acute retinal necrosis (ARN) is part of spectrum of necrotizing herpetic retinopathies, the clinical expression of which appears to be influenced by host and viral factors.

**Etiology**

1. Acute, fulminant disease may arise without a systemic prodrome years after primary infection or following cutaneous or systemic herpetic infection such as dermatomal zoster, chickenpox, or herpetic encephalitis (HSV-1 or -2).
2. Recent studies using PCR-based assays suggest that the most common cause of ARN is VZV infection, followed by infections with HSV-1, HSV-2, and, in rare instances, CMV.

**Epidemiology**

1. Originally described in 1971 among otherwise healthy adults, ARN has also been reported in children and among immunocompromised patients, including those with HIV infection.
2. The prevalence is nearly equal between the sexes.
3. Majority of cases cluster in patients between the fifth and seventh decades of life.
4. Patients with ARN caused by HSV-1 or VZV infection tend to be older (mean age, 40 years), whereas those with ARN due to HSV-2 infection tend to be younger (below age 25 years).



**Diagnostic criteria**

- The American Uveitis Society has established criteria for the diagnosis of ARN solely on the basis of clinical findings and disease progression, independent of viral etiology or host immune status

**Table 7-1 American Uveitis Society Criteria for Diagnosis of Acute Retinal Necrosis**

| |
|---|
| One or more foci of retinal necrosis with discrete borders, located in the peripheral retina* |
| Rapid progression in the absence of antiviral therapy |
| Circumferential spread |
| Occlusive vasculopathy with arteriolar involvement |
| Prominent vitritis, anterior chamber inflammation |
| Optic neuropathy/atrophy, scleritis, pain supportive but not required |

*Macular lesions do not exclude diagnosis in the presence of peripheral retinitis.

- Retinal lesions of presumed herpetic etiology that are not characteristic of well-recognized syndromes such as ARN, CMV retinitis, or progressive outer retinal necrosis are grouped under the umbrella designation necrotizing herpetic retinopathy.

## Clinical features

I. **Systemic features**

1. There is a higher risk of encephalitis and meningitis among patients with ARN caused by HSV-1 infection than by VZV infection.
2. ARN may occur following or simultaneously with Herpetic skin disease

II. **Ocular features**

**A. Symptoms**- Patients with ARN usually present with acute unilateral loss of vision, photophobia, floaters, and pain.

**B. Signs**

1. **Fellow eye involvement**
   - Occurs in approximately 36% of cases, usually within 6 weeks of disease onset.
   - Involvement may be delayed for extended periods (up to 26 years has been reported) after initial presentation

2. **Panuveitis** - It begins with

| | | | | |
|---|---|---|---|---|
| 1. Anterior segment inflammation | 2. KPs | 3. PS | 4. elevated IOP | 5. Heavy vitreous cellular infiltration |

3. **Triad** - Within 2 weeks, the classic triad of

| | | |
|---|---|---|
| 1. Occlusive retinal arteriolitis | 2. vitritis | 3. A multifocal yellow-white peripheral retinitis has evolved |

4. **Retinal involvement**
   - Early on, the peripheral retinal lesions are discontinuous and have scalloped edges that appear to arise in the outer retina.
   - Within days the lesions coalesce to form a confluent 360° creamy retinitis that progresses in a posterior direction, leaving full-thickness retinal necrosis, arteriolitis, phlebitis, and occasional retinal hemorrhage in its wake.

5. **Sequelae and complications**
   - Widespread necrosis of the midperipheral retina, multiple posterior retinal breaks, and proliferative vitreoretinopathy predispose eyes to combined tractional–rhegmatogenous retinal detachments in 75% of patients.
   - The posterior pole tends to be spared, but an exudative retinal detachment may arise with severe inflammation.
   - The optic nerve is frequently involved, as evidenced by disc swelling and a relative afferent pupillary defect.

## Differential diagnosis

| | | |
|---|---|---|
| 1. CMV retinitis<br>**2.** Syphilis | **3.** Atypical toxoplasmic retinochoroiditis - PORT<br>**4.** Autoimmune retinal vasculitis such as that of Bechet disease | 5. Lymphoma<br>**6.** Leukemia |

**Diagnosis**

A. In most instances, the diagnosis is made **clinically**.

B. **PCR**

1. When the diagnosis is uncertain, polymerase chain reaction (PCR) testing of aqueous and/or vitreous samples or retinal choroidal biopsy should be performed.
2. PCR testing is probably the most sensitive, specific, and rapid diagnostic method for detecting infectious posterior uveitis in general and ARN specifically.
3. It has largely supplanted viral culture, intraocular antibody titers, and serology.
4. PCR testing may be performed on either aqueous humor or vitreous biopsy specimens.
5. For most cases of ARN, aqueous sampling is usually sufficient.
6. Quantitative PCR may add additional information with respect to viral load, disease activity, and response to therapy.

**C. GW coefficient**

1. Intraocular antibody production as a measure of the host response to a specific microbial pathogen can be computed using the Goldmann-Witmer (GW) coefficient.
2. A ratio of greater than 3 is considered diagnostic of local antibody production.
3. Combining the GW coefficient with PCR analysis may increase diagnostic yield, especially in viral infections.

D. **Endoretinal biopsy**

- In rare instances in which PCR results are negative but the clinical suspicion for herpetic necrotizing retinitis is high, endoretinal biopsy may be diagnostic.

**Treatment**

**Role of treatment**

- Effective treatment inhibits the development of new lesions and promotes lesion regression over 4 days.
- Extended antiviral therapy may reduce the incidence of contralateral disease or bilateral ARN by 80% over 1 year.

A. **Intravenous acyclovir**

- **Induction therapy**
  1. 10 mg/kg every 8 hours for 10–14 days is effective against HSV and VZV.
     - Reversible elevations in levels of serum creatinine and liver enzymes may occur
     - In the presence of frank renal insufficiency, the dosage will need to be reduced.
  2. Oral valacyclovir at doses of up to 2 g 3 times daily has been used successfully as an alternative to intravenous acyclovir
- **Follow-on oral dose**- daily should be continued for 3 months VZV
  1. Acyclovir at 800 mg orally 5 times daily,
  2. Valacyclovir at 1 g orally 3 times daily,
  3. Or Famciclovir at 500 mg orally 3 times.
  4. For ARN associated with HSV-1 infection, the follow-on oral dose is one-half of that for VZV.

B. **Systemic corticosteroids** - After 24–48 hours of antiviral therapy, prednisone, 1 mg/kg/day are introduced to treat active inflammation and are subsequently tapered over several weeks.

C. **Aspirin and other anticoagulants** have been used to treat an associated hypercoagulable state and prevent vascular occlusions, but the results have been inconclusive.

D. **Intravitreal injections**

1. **Intravitreal ganciclovir (0.2–2.0 mg/0.1 mL) and foscarnet (1.2–2.4 mg/0.1 mL)** have been used to achieve a rapid induction in combination with both intravenous and oral antivirals as first-line therapy or for disease that fails to respond to systemic acyclovir.
2. High-dose systemic oral therapy, alone or in combination with intravitreal antiviral drugs, has not been demonstrated as superior to the classic intravenous approach.
3. Given the short intravitreal half-life of these drugs, injections may need to be repeated twice weekly until the retinitis is controlled.

E. **Prevention of RD**

1. Retinal detachment occurs within the first weeks to months following the onset of retinitis.
2. Given the location and multiplicity of retinal breaks, **prophylactic barrier laser photocoagulation,** applied to the areas of healthy retina at the posterior border of the necrotic lesions, may prevent retinal detachment and is recommended as soon as the view permits.
3. **Early vitrectomy combined with endolaser photocoagulation** has been proposed to help eliminate the contribution of vitreous traction on the necrotic retina.

F. **Treatment of RD**

- Due to the presence of proliferative vitreoretinopathy and multiple posterior retinal tears, internal repair

1. using vitrectomy techniques,
2. air–fluid exchange,
3. endolaser photocoagulation,
4. Or long-acting gas or silicone oil tamponade is more successful in achieving a higher rate of anatomical attachment than are standard scleral buckling procedures.

- Untreated, approximately two-thirds of eyes obtain a final visual acuity of 20/200 or worse because of retinal detachment, concurrent optic atrophy, or macular pathology.

**GW coefficient**

- The GW coefficient for a specific pathogen is calculated by dividing the amount of immunoglobulin G (IgG) reactive to a specific pathogen (xIgG) in aqueous by the total amount of IgG in the aqueous, and then dividing that ratio by a ratio created by dividing the amount of the same specific antigen IgG (xIgG) in serum by the total amount of IgG in serum:
- For example, in order to calculate the GW for Toxoplasma gondii, one would obtain both aqueous and serum samples and determines the amount of IgG reactive to T gondii (Toxoplasma IgG) in the aqueous and serum as well as the total amounts of IgG in aqueous and serum.
- Then the GW coefficient would be determined as follows:

$$GW = \frac{(\text{xIgG in aqueous/total IgG in aqueous})}{(\text{xIgG in serum/total IgG in serum})}$$

- A ratio of greater than 3 is considered diagnostic of local antibody production.