OPT- 243
Fluorescein & Indocyanine Angiography
– General Principles & Interpretation
Algorithm

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UAB Optometry
Fluorescein dye

- Safe; inert
- Has long track record - over 45 years
- Mixes with plasma and highlights blood vessel compromise
Fluorescein dye

- Using specific exciting (490 nm) and absorption (510 nm) filters...
  - B/W film documents vascular changes
  - Eliminated through liver and kidneys in 24-36 hours
- Stains skin and mucous membranes (24-36)
Fluorescein dye

- May contaminate results of urine tests for reducing sugars (up to 4-5 days)
- Does not diffuse through NORMAL retinal blood vessels
- Normally leaky choroidal vessels show uniform “choroidal flush”
Complications of FA

- Mild
  - Nausea, sneezing
  - Pruritis
  - Vomiting
  - Extravasation at injection site
Complications of FA

- Moderate
  - Urticaria (< 2%)
  - Syncope (< 0.2%)
  - Other (< 0.006%)
    - Skin eruptions
    - Thrombophelibitis
    - Pyrexia
    - Focal tissue necrosis
    - Nerve palsy
Complications of FA

- **Severe**
  - Respiratory events (< 0.0003%)
    - Laryngeal edema
    - Bronchospasm
    - Anaphylaxis
  - Cardiovascular events (< 0.0002%)
    - Circulatory shock
    - Cardiac arrest
Contraindications

- Previous anaphylactic reaction
- Other previous reactions - weigh risk:benefit
- Kidney disease (relative contraindication)
- Pregnancy
  - Avoid, especially during the first trimester
Clinical Blood – Retinal Barrier

- Inner
  - Vascular endothelium (integrity)

- Outer
  - Retinal Pigment Epithelium
Histological analog of a normal angiogram

Thomas Freddo, OD, Ph.D.
Inner Blood-Retinal Barrier
Retinal capillaries are sealed by tight junctions.

Outer Blood-Retinal Barrier

Choroidal capillaries are fenestrated and therefore leak fluid, ions & plasma proteins.

RPE cells have tight junctions that prevent these substances from diffusing into the retina.
Retinal Capillaries

Retinal capillaries are non-fenestrated. Using intravascular tracers, that mimic the behavior of plasma proteins, retinal capillaries are impermeable and these proteins do not diffuse into the surrounding retina.
Choriocapillaris

Choroidal capillaries are fenestrated (arrowheads). Using intravascular tracers, that mimic the behavior of plasma proteins, choroidal capillaries are freely permeable and these proteins diffuse into the surrounding choroidal stroma.

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Retinal Pigmented Epithelium

RPE cells are joined by tight junctions. This histological slide illustrates the use of intravascular tracers, that mimic the behavior of plasma proteins, showing the intercellular spaces between RPE cells to be impermeable to these proteins.

Thomas Freddo, OD, Ph.D.
Summary of the Blood-Retinal Barrier

- *Tight junctions* between retinal vascular endothelial cells prevent plasma proteins from diffusing into the retina.

- *Tight junctions* between RPE cells prevent plasma proteins that have leaked from the fenestrated choroidal capillaries from diffusing into the retina.
Routes of Administration

- Oral (shows only late leakage by angioscopy)
  - May be applicable in children or where IV route is impossible
  - Shows only late stage; not circulation phases (angioscopy)

- Intravenous (IV) - shows transit of fluorescein as blood circulates and re-circulates
Indications

- **FA is employed to support diagnoses and direct treatment**
- Examples of conditions that may be amenable to treatment (e.g., photocoagulation)
  - Diabetic macular edema
  - Age-related macular degeneration
  - Other diseases that have neovascularization or macular edema as a consequence
Normal re-circulation times

- Arm to retina: 10-15 [7.5-25] sec  *(via???)*
- Arterial retinal: 0.9-1.1
- Venous retinal: 1.7-2.2
- Total retinal: 2.6-3.3

*total transit time can be up to ~ 30 sec*
Arm to retina times

- Reduced in youth and anemia
- Prolonged (slow/impaired blood flow)
  - Carotid stenosis
  - Sludging disorders
Procedure

- Color fundus photo
- Red-free photo (reference)
- Camera ready (SLO, also)

Patient prep
  - Injection site
  - Syringe w/5 ml (10%); injected into the antecubital vein (3-7 sec as bolus)
Procedure

- Photographic sequence
  - 2-3 frames/10-12 sec
  - Then every 2 – 3 sec for next 10 sec
  - Late frames @ 5 to 20 minutes
Fluorescein Angiography
Phases of an Angiogram

- Choroidal flush (prearterial)
- Early Phase (arterial)
- Mid Phase (arteriovenous, venous, laminar)
- Late Phase (recirculatory)
Choroidal flush (prearterial)

- The initial arm-to retina time is recorded as the first appearance of fluorescein in the choroidal vasculature system (10-20 sec)
- Uniform glow from permeable choroidal circulation
- Cilioretinal artery fills
Phases of an Angiogram

Early Phase (arterial)

- The arteries alone in the retinal vascular tree are visibly filled with fluorescein against the choroidal flush

*Note: a cilioretinal artery fills with the choroidal circulation*
Early Phase (arteriovenous)
Why is the macula dark?
Why are the veins filling at their edges?
Phases of an Angiogram

Early / Mid Phase
(arteriovenous, venous; 3-5 min)

- Early filling of the veins, laminar flow, or border filling of the veins (*looks like railroad tracks*), followed by...

- Arteries and veins fully filled with fluorescein
Early / Mid Phase - venous
Phases of an Angiogram

The Late Phase

- This phase is documented 5-20 min following injection
- In normals, no staining or leakage is seen
- Abnormal results include late leakage not contained by the circulation, or staining
Late Phase
Interpretation of an Angiogram

- **Hyper fluorescence** – leakage of neovascularization in (wet) AMD, pooling in central serous choroiretinopathy

- **Hypofluorescence** – an ischemic territory in vein occlusion (absence)

- **Blocked fluorescence** – by overlying retinal blood blocking the uniform appearance of the choroidal flush

- **Late staining** – cystoid macular edema, choroidal malignant melanoma
Interpretation of an Angiogram

- **Autofluorescence**
  - Natural glow of ocular tissues without fluorescein (e.g., optic nerve drusen, astrocytoma)

- **Pseudofluorescence**
  - May be due to unbalanced photographic filter system
  - Also used to describe the margin of scar tissue (e.g., fibrovascular scarring of AMD)
Interpretation Strategies / Examples

- FIRST - compare the color and R/F photos

- NEXT - identify the stage of the angiogram

- Look for one of the 4 characteristic abnormalities (hyper-, hypo-, blocked or late-phase staining/leakage)
Interpretation Strategies / Examples

- Determine if the abnormal fluorescence is changing or remaining the same throughout the angiogram.
- Correlate the anatomical (clinical) and angiographic sites; again refer to the color and R/F photos.
- !!! FA is to confirm diagnoses and guide treatment; not to make a diagnosis.
Fluorescein Angiography and the compromised B-R-B

DX: BRVO
Abnormal examples
A: 1. CWS in papillomacular bundle
2. Intraretinal hemorrhage

B: FA
1. capillary nonperfusion in the area corresponding to the cotton-wool patch; 2. blocked fluorescence caused by the intraretinal hemorrhage

Yanoff and Duker in MD consult

Healthy 37 YO M

- 3-hour history of visual loss (VA 20/60).

A: Retinal whitening is very subtle and the retinal vessels appear normal.

(B) FA reveals abnormal arterial filling. (confirming CRAO)

Indications (Reminder!)

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Video Fluorescein Angiogram

http://www.medivision.co.il/dfi.htm
Indocyanine Green Angiography

- ICG (tricarbocyanine)
- Near IR (780/810 nm) absorption/emission
- Similar injection protocol / safety spectrum to fluorescein, ex:
  - metabolized in liver
  - contains iodine
- Advantages
  - Defines CNV better than FA
  - Visualization improved through media opacities, pigment, blood, and scar tissue
Indocyanine Green Angiography

- Most useful for choroidal filling assessment
- ∴ application in AMD
- Example
ICG in AMD

ICG absorbs and fluoresces in the near IR improving choroidal visibility and diffuses more slowly from the choriocapillaris

68 W/M; 20/30 (color)

Prolonged choroidal filling (1 min FA)

1 min ICGA

3 min ICGA

Reduced diffuse background fluorescence
ICGA - 72 W/F 20/20 early AMD

Prolonged choroidal filling (PCF) more evident on ICGA
Examples of Fluorescein Angiograms

- Normal Angiogram
- Diabetic Retinopathy (NPDR)
- Proliferative Diabetic Retinopathy (PDR)
- Age-related Macular Degeneration (AMD)
Normal Posterior Pole / FA

Fig. 8. Fundus photograph (A) and fluorescence angiogram (B) of normal eye. Normal retinal vessels are present.
Arrowheads = intraretinal hard exudates
Arrows on FA = surrounding areas of leaking microaneurysms
FA in diabetic retinopathy
FA in diabetic retinopathy
FA in diabetic retinopathy
BLACK Arrow = PDR at ONH, w/ corresponding leakage on FA
WHITE arrow = microaneurysms

A.N. Witmer et al. / Progress in Retinal and Eye Research 22 (2003) 1–29
Neovascular AMD \(* = \) CNVM; hard exudates are also present.
Black arrow on FA = leakage from NV.