ANTIPLATELET AGENTS VS. ANTICOAGULATION FOR STROKE & TIA

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Learning Objectives

- Describe the two main ways that blood clots using nonmedical terms
- List the 6 ischemic stroke etiologies
- Determine the optimal antithrombotic therapy for secondary prevention of ischemic stroke based on ischemic stroke etiology
- Relate the rationale for prescribing anticoagulation rather than antiplatelet agents in patients with ischemic stroke of unknown cause
THE BLOOD

Unique substance that fluctuates between two forms

- Liquid – to transport blood cells, oxygen, glucose, other chemistries, etc. within the vascular system
- Glue – to seal injured artery or vein & prevent blood loss
  - Scab & clot (= thrombus) are examples of blood as glue
  - Glue (scab/clot) forms for 1 of 2 reasons:
    - **Platelets (white clot)** – like Velcro
      - Stick to bumpy surfaces inside arteries
      - If the inner lining of the artery (endothelium) is normal, platelets do NOT cause thrombus formation
    - **Clotting factors (red clot)** – like powdered Jello
      - Exist in balance with natural blood thinners
      - Clump when blood is stagnant or when unopposed by natural blood thinners
**BLOOD-THINNING THERAPY**

- *Antithrombotic therapy* is a general term for all blood-thinning medications
- There are 2 types of antithrombotic therapy
  - *Antiplatelet agents* – anti-Velcro medicines
  - *Anticoagulants* – anti-Jello medicines
ISCHEMIC STROKE & TIA PATHOPHYSIOLOGY

Ischemia (low blood flow) to focal area of brain

- Usually due to **thromboembolus (floating blood clot)**
  - Thrombus = blood clot
  - Embolus = floating plug
  - Blood clot forms in vascular system (arteries or heart), travels downstream, plugs a brain artery

- Blood clots come from 1 of 3 locations:
  - **Artery** – esp. hardening of artery wall (atherosclerosis)
  - **Heart** – esp. irregular heart rhythm (atrial fibrillation)
  - **Blood** – blood abnormally sticky (hypercoagulable state)
FOCAL CEREBRAL ISCHEMIA

Both usually due to thromboembolism—both are emergencies!

- **Acute ischemic stroke (AIS)**
  - Focal brain ischemia with infarction, usually with sequelae, because clot did not dissolve in time
  - Equivalent term is “cerebral infarction”

- **Transient ischemic attack (TIA)**
  - Focal brain ischemia with transient episode of neurologic dysfunction—but NO infarction or sequelae, because clot dissolved in time
  - Signals that patient is at risk for ischemic stroke in the near future—next time, the clot may not dissolve in time
  - Partial seizures and migraines can mimic TIAs

*Etiologic evaluation (i.e., source & type of clot) determines appropriate long-term antithrombotic therapy to prevent future strokes*
URGENT ANTITHROMBOTIC THERAPY IN AIS

May have to administer rectally (ASA) or via NG feeding tube

Begin some form of antithrombotic therapy within 48 h of AIS onset—but change to definitive antithrombotic therapy after etiologic evaluation

- Aspirin (ASA) 325 mg/d*
  - Begun within 48 h of stroke onset ↓s morbidity & mortality (avoid enteric coating rectally or via NG tube)

- Aspirin (ASA) + Clopidogrel (CLO) – consider if suspected large-artery disease etiology of ischemic stroke**
  - ASA 325 mg/d x 90 d
  - CLO 300 mg x 1, then 75 mg/d x 90 d
  - After 90 d, discontinue either ASA or CLO

But delay start of all antithrombotic therapy x 24 h after tPA administration

*From IST (Lancet 1997;349:1569-1581)

**Modified after 2 trials: CHANCE (NEJM 2013;369:11-19) & SAMMPRIS (NEJM 2011;365:993-1003)
ISCHEMIC STROKE ETIOLOGIES
In North American & European Studies*

Using the TOAST Classification**

- **LAA** – Large-artery atherosclerosis
- **SAD** – Small-artery disease
- **CE** – Cardioembolism
- **OTH** – Other determined cause
- **UND** – Undetermined cause

**Adams HP Jr et al. Stroke 1993; 24:35-41
ISCHEMIC STROKE ETIOLOGIES
The 6 Causes of Ischemic Stroke

Using Modified TOAST Classification
After elimination of “undetermined” & division of “other” into 3 categories

- **LAA** – Large-artery atherosclerosis
- **SAD** – Small-artery disease
- **CE** – Cardioembolism
- **NAV** – Nonatherosclerotic vasculopathies
- **HCS** – Hypercoagulable states
- **HP** – Hypoperfusion

Percentages are estimates based on literature & personal experience
LARGE-ARTERY ATHEROSCLEROSIS

- “Hardening of the arteries” after many (> 20) years of risk factors
  - Advanced age
  - Hypertension
  - Diabetes mellitus
  - Hypercholesterolemia
  - Cigarette smoking

- Atherosclerosis is likely cause of ischemic stroke if:
  - > 50% arterial stenosis by catheter angiography
  - > 70% arterial stenosis by carotid duplex ultrasound, CTA, or MRA
  - Aortic arch plaque > 4 mm by transesophageal echo (TEE)

- Due to Velcro (white-clot/platelet) thromboembolus
  - Platelets stick to bumpy plaque and form a thrombus that breaks off to form an embolus that floats downstream and blocks a brain artery

- Treat with antiplatelet agent(s), aspirin or clopidogrel (or both for limited duration such as 3 months after stroke/TIA)

CTA = CT angiography; MRA = MR angiography
SMALL-ARTERY DISEASE (LACUNAR STROKE)

- To diagnose, patient must meet all 5 criteria:
  - Hypertension or diabetes for many (> 20) years
  - Lesion in middle part of brain or brainstem
  - Small infarct size ≤ 1.5 cm
  - “Lacunar” clinical syndrome
    - Pure motor, pure sensory, pure sensorimotor
    - Dysarthria-clumsy hand, ataxic hemiparesis, hemiballismus
  - No potential large-artery or cardiac source
    - Not all small-artery infarctions are due to small-artery disease
    - All 5 other ischemic-stroke etiologies can cause small-artery infarctions
    - Small-artery “disease” is a diagnosis of exclusion
- Due to Velcro (white-clot/platelet) thrombus
- Treat with antiplatelet agent, esp. aspirin (combining aspirin & clopidogrel is NOT helpful in small-artery disease)
CARDIOEMBOLISM

- Usually occurs when previous cardiac disease leads to stasis (stagnation) of blood in a heart chamber, for example:
  - Atrial fibrillation or flutter
  - Akinetic left ventricular wall from myocardial infarction—esp. AWMI w/in 48 h
  - Dilated cardiomyopathy – esp. ejection fraction < 35%
  - Mechanical prosthetic valve – only use warfarin with target INR 2.5-3.5
  - Spontaneous echo contrast (= SEC = “smoke”)—swirling microclots seen on echocardiography, suggesting stasis
  - Patent foramen ovale (PFO) – closure does not ↓ stroke risk
  - Interatrial septal aneurysm (IASA) – esp. if ≥ 5 mm & associated with PFO

- Due to Jello (red-clot/clotting factor) thromboembolus
  - Stasis of blood in poorly pumping heart chamber causes clotting factors to form a thrombus that breaks off to form an embolus that floats downstream & blocks a brain artery

- Treat w/ anticoagulant—novel oral anticoagulant (NOAC) or warfarin

_Rarely, cardioemboli are NOT made of thrombi, e.g., intracardiac tumors embolize tumor debris & subacute bacterial endocarditis embolizes pus_
NONATHEROSCLEROTIC VASCULOPATHY

Carotid & vertebral artery dissection

- **Neck trauma** often responsible (whiplash, hyperextension, twisting, compression, manipulation)
- **Intimal tear** → blood between intima & media → tubular stenosis or tapered occlusion of artery + thromboemboli
- **Head and/or neck pain** common & may be only symptom
  - Carotid dissection – throat, peri-auricular pain; Horner synd.
  - Vertebrobasilar dissection – occipital, neck pain
- **Anticoagulation** x 3 months, then aspirin 81-325 mg/d (evidence limited)

![Images of blood vessels with normal and dissection views](image1.jpg)
![Images of MRI showing abnormal periarterial signal](image2.jpg)
NONATHEROSCLEROTIC VASCULOPATHIES

Moyamoya disease & CADASIL

- **Moyamoya disease** (moyamoya = “puff of smoke” in Japanese)
  - Thickening of distal ICA, proximal MCA, proximal ACA
  - Small arteries in basal ganglia grow (“puff of smoke” on arteriography)
  - Affects children, young adults; female > male 2:1
  - Migraine, TIA, ischemic stroke, esp. in younger patients
  - Intracerebral hemorrhage in older patients (30s & 40s)
  - External carotid-internal carotid (EC-IC) bypass surgery
  - *Aspirin 81-325 mg/d*

- **CADASIL**
  - Acronym for “Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarctions & Leukoencephalopathy”
  - Smooth muscle pathology; NOTCH 3 gene mutation on chromosome 19
  - Migraine, TIA, & small, subcortical ischemic strokes
  - *Aspirin 81-325 mg/d*
NONATHEROSCLEROTIC VASCULOPATHIES

*Migraine, vasculitis, sickle-cell, FMD*

- **Migraine-related infarction**
  - Due to migraine with aura & underlying hypercoagulable state
  - *NOAC*

- **Cerebral vasculitis** (primary CNS & secondary systemic forms)
  - Very rare; affects children & young adults
  - Delirium & seizures due to multiple concurrent small infarctions
  - Immunosuppressive therapy
  - *NO antithrombotic therapy*

- **Sickle-cell disease**
  - Transfuse to maintain Hgb S < 30%
  - *Aspirin 81 mg/d*

- **Fibromuscular dysplasia (FMD)**
  - Rare; “beaded” arteries on angiography; female >> male
  - *Aspirin 81-325 mg/d*
HYPERCOAGULABLE STATES (THROMBOPHILIA)

- Excessive blood clotting, even in normal arteries or veins
- Most often due to dysfunction of clotting factors (a Jello problem) & thus, treatment is usually anticoagulation
- **Two-hit phenomenon** often needed to become symptomatic
  - Often, hypercoagulable states (HCS) cause thrombosis only when the patient has 2 simultaneous conditions that promote clotting such as:
    - Inherited HCS + acquired HCS
    - Two acquired HCS
    - HCS + dehydration
    - HCS + estrogen or testosterone therapy
    - HCS + atrial septal abnormality (PFO &/or IASA)
    - HCS + prolonged migraine aura
  - This explains why an inherited (genetic) HCS may be asymptomatic for many years before resulting in ischemic stroke
HYPERCOAGULABLE STATES

Incomplete evaluations lead to self-fulfilling prophecy

25% of ischemic strokes are said to be of “unknown cause,” yet, even at leading medical institutions, hypercoagulable profiles are often performed incompletely or not at all

- Stepwise approach:
  - Less expensive, but...
  - Likely to miss multifactorial cause

- Comprehensive profile:
  - More expensive, but...
  - Provides better information regarding need for long-term anticoagulation

Incomplete evaluations due to cost concerns lead to underestimates of incidence & skepticism regarding HCS as cause of stroke
HYPERCOAGULABLE STATES

Clinical clues to their presence in ischemic stroke patients

- Child or young adult (especially ≤ 55 years old)
- Ischemic stroke of undetermined cause
  - Arterial studies normal AND...
  - Heart studies normal or just show PFO or IASA
- Personal or family history of systemic clotting:
  - Myocardial infarction at young age
  - Ischemic stroke at young age
  - Idiopathic cardiomyopathy
  - Deep vein thromboses
  - Pulmonary emboli
  - Miscarriages
  - Other
HYPERCOAGULABLE STATES

A possible explanation for the Stroke Belt?

- **Stroke Belt** = region of the southeastern U.S. in which the rates of both stroke mortality and recurrent ischemic stroke are higher for all citizens of regardless of gender or race

- **Reason for U.S. Stroke Belt is a mystery**, but it must be:
  - Due to ischemic stroke (since there is a parallel “Heart Attack Belt”)
  - Due to stroke in young adults (since data are age-adjusted)
  - NOT related to atherosclerosis or traditional vascular risk factors
  - NOT likely to be discovered on routine stroke etiologic evaluations
  - NOT prevented with antiplatelet agents (current treatment of choice for stroke of unknown cause)

- **We have theorized that U.S. Stroke Belt is due to an increased prevalence of hypercoagulable states in the region**
HYPERCOAGULABLE STATES

Conditions that may cause ischemic stroke through excessive clotting

• Excessive clotting factors
  – Fibrinogen
  – Factor VII
  – Factor VIII
  – Factor XI

• Deficient natural anticoagulants
  – Antithrombin III
  – Protein C
  – Protein S (total & free)

• Genetic mutations (hetero- or homozygote)
  – Activated protein C resistance = APCR
  – Leiden factor V (a cause of APCR)
  – Prothrombin G20210A
  – Methylene tetrahydrofolate reductase (MTHFR) 655CT (C677T) & 1286AT (A1298C)

• Autoimmune phenomena (antiphospholipid antibodies)
  – Lupus anticoagulant
  – Anticardiolipin antibodies (Abs)
  – Anti-β-2-glycoprotein I Abs
  – Antiphosphatidylserine Abs

• Other
  – Elevated lipoprotein (a) ≥ 30
  – Sickle cell screen

• Systemic conditions
  – Dehydration
  – Acute infection/inflammation
  – Nephrotic syndrome
  – Inflammatory bowel disease
  – Paraneoplastic syndrome
  – Thrombocythemia
HYPOPERFUSION

Acute hypotension may cause ischemic stroke

WATERSHED (BORDERZONE) INFARCTION

Usually due to inappropriately rapid BP lowering by a physician—not embolism

Sudden or excessive drop in blood pressure may cause a drop in cerebral perfusion pressure & insufficient blood flow to cover distal arterial territories with resultant infarction of tissues between artery territories, just as a drop in water pressure results in death of the grass between sprinkler zones

Prescribing clonidine PRN or sending someone to the ED for hypertensive urgency is more likely to cause stroke than to prevent one.

Long-term antithrombotic therapy generally not indicated for these patients.
ISCHEMIC STROKE OF UNKNOWN ETIOLOGY

- Up to 25% of ischemic strokes are of unknown cause
- Two ischemic stroke etiologies may escape work-ups:
  - **Hypercoagulable states** – need to obtain special tests
  - **Intermittent arrhythmias** – may need long-term monitoring (≥ 21 d) with implantable device
- **Growing sentiment to treat with anticoagulation**
  - For lifetime in most, but at least for first 3 months
  - Reconsider after hypercoagulable profile and/or long-term cardiac monitoring results are available

*Healey et al. 2012
Hart et al. 2014*
## AIS/TIA Etiologic Evaluation

Determine clot origin (artery, heart, or blood)

<table>
<thead>
<tr>
<th>NONINVASIVE Day 1</th>
<th>INVASIVE Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAIN</td>
<td></td>
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<tr>
<td>MRI (w/ DWI, ADC, &amp; FLAIR) (DWI &amp; ADC show very early ischemia)</td>
<td></td>
</tr>
<tr>
<td>ARTERIES</td>
<td></td>
</tr>
<tr>
<td>CTA head &amp; neck (both with IV contrast) or MRA head &amp; carotid duplex (CD) (neither with IV contrast)</td>
<td>Catheter angiography* (to clarify findings on CTA, MRA, or CD)</td>
</tr>
<tr>
<td>HEART</td>
<td></td>
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<tr>
<td>ECG &amp; monitor Cardiac biomarkers Transthoracic echo (TTE) (TTE for left ventricular source)</td>
<td>Transesophageal echo (TEE)* (TEE for left atrial, atrial septal, aortic arch sources)</td>
</tr>
<tr>
<td>BLOOD</td>
<td></td>
</tr>
<tr>
<td>Hypercoagulable profile* (perform day 3 if artery &amp; heart evaluations negative)</td>
<td>*in select patients</td>
</tr>
</tbody>
</table>

*OU Neurology*
AIS/TIA SECONDARY PREVENTION
Type of clot—Velcro vs. Jello—determines antithrombotic therapy

HIGH-FLOW STATES
- Large-artery Atherosclerosis
- Small-artery Disease

Platelets (Velcro)
Platelets—like VELCRO—adhere to atherosclerotic plaque on arterial wall to form WHITE clots

LOW-FLOW STATES
- Cardioembolism
- Hypercoagulable State

Clotting factors (Jello)
Clotting factors—like powdered JELLO—coalesce in stagnant heart chambers or vessels to form RED clots

ANTIPLATELET AGENT
ANTICOAGULANT

Some patients need both types of antithrombotic therapy, e.g., a patient with coronary artery disease & atrial fibrillation
ANTIPLATELET AGENTS
Mechanisms of Action

- **Aspirin**
  - **Permanently** inhibits cyclo-oxygenase (COX)
  - Goal is to inhibit platelet COX, but not endothelium COX
    - Platelet COX makes thromboxane (prothrombotic)
    - Endothelium COX makes prostacyclin (antithrombotic)
    - Low doses (81-1300 mg/d), selectively inhibit platelet COX

- **Clopidogrel**
  - Inhibits ADP-mediated platelet aggregation
  - Inhibits binding of platelet glycoprotein receptors to fibrinogen
ANTIPLATELET AGENTS
Aspirin Practical Considerations

- Dose: 81 mg to 325 mg/day
- 325 mg/d is preferred in certain circumstances
  - Acute phase of ischemic stroke (within 48 h of admission)
  - Atrial fibrillation in patients who cannot take anticoagulant
  - Combined with clopidogrel for specified duration
- > 1300 mg/day is NOT effective for blood thinning
- NSAIDs may decrease blood-thinning effectiveness
ANTIPLATELET AGENTS

Clopidogrel Practical Considerations

- Dose: 75 mg/day (+/- initial loading dose of 300 mg)
- Proton pump inhibitors may decrease effectiveness
- Atorvastatin may decrease effectiveness
- Some patients have genetic resistance
- VerifyNow testing may assess efficacy
ANTIPLATELET AGENTS

Indications for Dual Antiplatelet Use

- After stent placement (duration varies)
  - Coronary (drug-eluting) stent – 12 months
  - Carotid (bare-metal) stent – 30-90 d

- After AIS/TIA due to atherosclerosis (for 90 d)
  - Intracranial stenosis > 50%
  - Significant, but nonstenotic atherosclerosis
  - Aortoembolism

Do not continue dual antiplatelet therapy indefinitely—
increases cerebral bleeding risk without decreasing
ischemic stroke risk
ANTICOAGULANTS
Mechanisms of Action

- **Warfarin (Coumadin)**
  - Inhibits synthesis of vitamin K-dependent clotting factors (II, VII, IX, X)

- **NOACs (novel oral anticoagulants)**
  - Dabigatran (Pradaxa) – reversible factor II inhibitor
  - Apixaban (Eliquis)
  - Rivaroxaban (Xarelto) – direct factor Xa inhibitors
  - Edoxaban (Savaysa)
ANTICOAGULANTS

Warfarin Practical Considerations

- Metabolized by liver
- Many food & drug interactions
- Long half-life of 20-60 h
  - *Slow onset*—*takes days to become effective*
  - *Hold 5-10 days before invasive procedure*
- Narrow therapeutic index drug
  - *Small changes in dose may lead to big changes in INR*
- Complications:
  - Warfarin skin necrosis – esp. w/ high loading dose, protein C/S deficiency
  - Blue toe/purple toe syndrome – assoc. w/ aortic arch atherosclerosis
- Target INR 2.0-3.0 in most patients
- *Target INR 2.5-3.5 for mechanical heart valve pts*
- Antidotes: vitamin K, fresh frozen plasma (FFP)
ANTICOAGULANTS

NOAC Practical Considerations 1 of 2

All NOACs are fixed doses without blood tests

- **Dabigatran** – 150 mg twice daily
  - May cause intolerable gastroesophageal reflux
  - Antidote: idarucizumab (Praxbind)

- **Apixaban** – 5 mg twice daily
  - Major bleed/intracranial hemorrhage risk < warfarin

- **Rivaroxaban** – 20 mg daily
  - Major bleed/intracranial hemorrhage risk = warfarin

- **Edoxaban** – 60 mg daily
  - Only use if renal dysfunction (creatinine clearance < 95 ml/min)
ANTICOAGULANTS

NOAC Practical Considerations 2 of 2

All NOACs:

- Efficacy > warfarin
- Minimal drug interactions
- Prominent urinary excretion
- Decrease dose for low GFR (glomerular filtration rate)
- Relatively short half-life 10-17 h
- Rapid onset (never need bridging therapy)
- Hold only 48-72 h before invasive procedure
ANTITHROMBOTIC AGENTS

Indications for both antiplatelet agent & anticoagulant

- Coronary artery disease/myocardial infarction +
  - Atrial fibrillation
  - Akinetic left ventricular wall
  - Dilated cardiomyopathy
  - Hypercoagulable state
- Aortoembolism with mural thrombus
- Mechanical heart valve patient with AIS or TIA despite INR 2.5-3.5
EXTRACRANIAL CAROTID STENOSIS

**NASCET measurement criteria**

- To assess stenosis, use the **catheter angiography** view with the highest-grade stenosis.
- Denominator is based on ICA just distal to the carotid bulb where walls begin to be parallel (D).
- % opening is N/D

\[
\text{% stenosis} = \frac{D - N}{D}
\]

*NASCET = North American Symptomatic Carotid Endarterectomy Trial*
AIS/TIA SECONDARY PREVENTION: ARTERIAL STENOSES (NARROWINGS)

EXTRACRANIAL CAROTID STENOSIS

- Procedure indicated only if stenosis:
  - > 50% by catheter angiography using NASCET criteria
  - > 70% by duplex, CTA, or MRA
- Options are:
  - Carotid endarterectomy + aspirin 81-325 mg/d
  - Carotid angioplasty & stenting + aspirin 325 mg/d + clopidogrel 75 mg/d x 30-90 d

INTRACRANIAL ARTERIAL STENOSIS

- Procedure NOT indicated
- Outcomes for optimal medical therapy alone MUCH BETTER than medical + angioplasty & stenting
- Optimal medical therapy =
  - Aspirin 325 mg/d
  - Clopidogrel 75 mg/d x 90 d
  - LDL < 70 with statin
  - SBP < 130

NASCET & Brott et al. 2010 (CREST)  Chimowitz et al. 2011 (SAMMPRIS)
AIS/TIA SECONDARY PREVENTION

Risk factors vs. cause—and hypercoagulability

- All ischemic strokes have a cause—know it or find it!
- Risk factors are not causes—if patient has no arterial or cardiac disease, risk factors are unrelated to stroke
- Don’t forget transesophageal echocardiogram, hypercoagulable profile, & long-term cardiac monitoring if initial tests don’t find a cause
- Suspect hypercoagulable state in:
  - All patients with no identifiable arterial or cardiac cause
  - All patients with “only” cause atrial septal abnormality (PFO, IASA)
  - Patients with strong personal or family history of clotting at young age, including miscarriages
  - Most (if not all) young patients (cutoff 55 to 60)
## ANTITHROMBOTIC THERAPY

### Recommendations for Secondary Stroke Prevention

### LARGE-ARTERY ATHEROSCLEROSIS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>After carotid endarterectomy</td>
<td>aspirin 81-325 mg/d</td>
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<tr>
<td>After carotid angioplasty &amp; stenting</td>
<td>aspirin 325 mg/d indefinitely + clopidogrel 300 mg x 1, then clopidogrel 75 mg/d x 90 d</td>
</tr>
<tr>
<td>Intracranial atherosclerosis</td>
<td>aspirin 81-325 mg/d indefinitely + NOAC until thrombus resolved on TEE</td>
</tr>
<tr>
<td>Aortoembolism <em>without</em> mural thrombus</td>
<td></td>
</tr>
<tr>
<td>Aortoembolism <em>with</em> mural thrombus</td>
<td></td>
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</tbody>
</table>

### SMALL-ARTERY DISEASE

<table>
<thead>
<tr>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>aspirin 81-325 mg/d or clopidogrel 75 mg/d (NEVER both)</td>
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</tbody>
</table>
# ANTITHROMBOTIC THERAPY

## Recommendations for Secondary Stroke Prevention

| **CARDIOEMBOLISM** | 
|-------------------|--------------------------------------------------|
| Atrial fibrillation or flutter | NOAC (or aspirin 325 mg/d if anticoagulant contraindicated) |
| Akinetic left ventricular wall | NOAC + aspirin 81 mg/d |
| Dilated cardiomyopathy (EF < 35%) | NOAC |
| PFO / IASA | NOAC (& obtain hypercoagulable profile) |
| Mechanical prosthetic heart valve | warfarin INR 2.5-3.5 +/- aspirin 81 mg/d |
| Subacute bacterial endocarditis | none (intravenous antibiotics) |
| Cardiac tumor | none (surgically resect tumor) |

<table>
<thead>
<tr>
<th><strong>HYPERCOAGULABLE STATES</strong></th>
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<tbody>
<tr>
<td>All except for thrombocythemia</td>
</tr>
<tr>
<td>Essential thrombocythemia</td>
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</table>
# ANTITHROMBOTIC THERAPY

**Recommendations for Secondary Stroke Prevention**

<table>
<thead>
<tr>
<th>NONATHEROSCLEROTIC VASCULOPATHIES</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Carotid or vertebral dissection</td>
<td>NOAC x 90 d, then aspirin 81-325 mg/d</td>
</tr>
<tr>
<td>Moyamoya disease</td>
<td>aspirin 81-325 mg/d (&amp; EC-IC bypass surgery)</td>
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<td>CADASIL</td>
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<td>Fibromuscular dysplasia</td>
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<td>Migraine-related infarction</td>
<td>NOAC (&amp; obtain hypercoagulable profile)</td>
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<tr>
<td>Cerebral vasculitis</td>
<td>none (immunosuppressive therapy)</td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td>aspirin 81 mg/d (&amp; transfuse Hgb S &lt; 30%)</td>
</tr>
<tr>
<td>Aortic arch dissection</td>
<td>none (lower blood pressure, surgical repair)</td>
</tr>
</tbody>
</table>

### HYPOPERFUSION

none (avoid sudden drops in blood pressure)
ANTIPLATELET AGENTS VS. ANTICOAGULATION FOR STROKE & TIA

REFERENCES 1 of 3

- Diener HC et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomized, double-blind, placebo-controlled trial. Lancet 2004;364:331-337 (MATCH)


REFERENCES 3 of 3

- Taylor DW et al. Low-dose and high-dose acetylsalicylic acid for patients undergoing carotid endarterectomy: a randomized controlled trial. Lancet 1999;353:2179-2184. (ACE)

Learning Objectives

- Describe the two main ways that blood clots using nonmedical terms
- List the 6 ischemic stroke etiologies
- Determine the optimal antithrombotic therapy for secondary prevention of ischemic stroke based on ischemic stroke etiology
- Relate the rationale for prescribing anticoagulation rather than antiplatelet agents in patients with ischemic stroke of unknown cause
THE END