Evaluation and management of rheumatologic emergencies in the ICU

DM Seminar:
Dr.Vamsi Krishna
Dept. of Pulmonary medicine

Rheumatologic emergencies

- 19% of emergencies admitted to acute general medical wards have rheumatological problem as the cause for admission

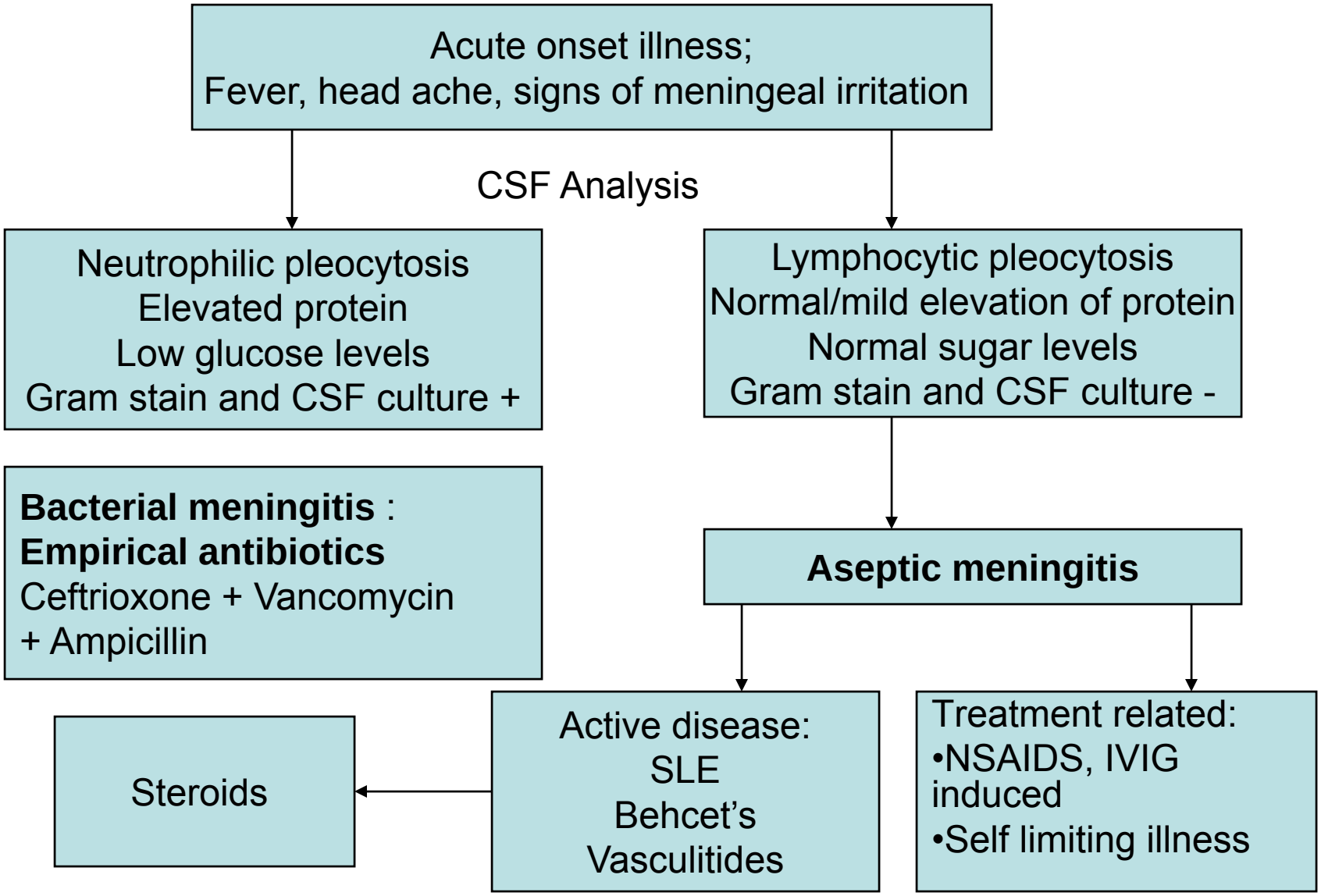
Spencer MA.Rheumatol Rehabil. 1981;20(2):71-3

- Complications of rheumatic diseases frequently present with protean manifestations

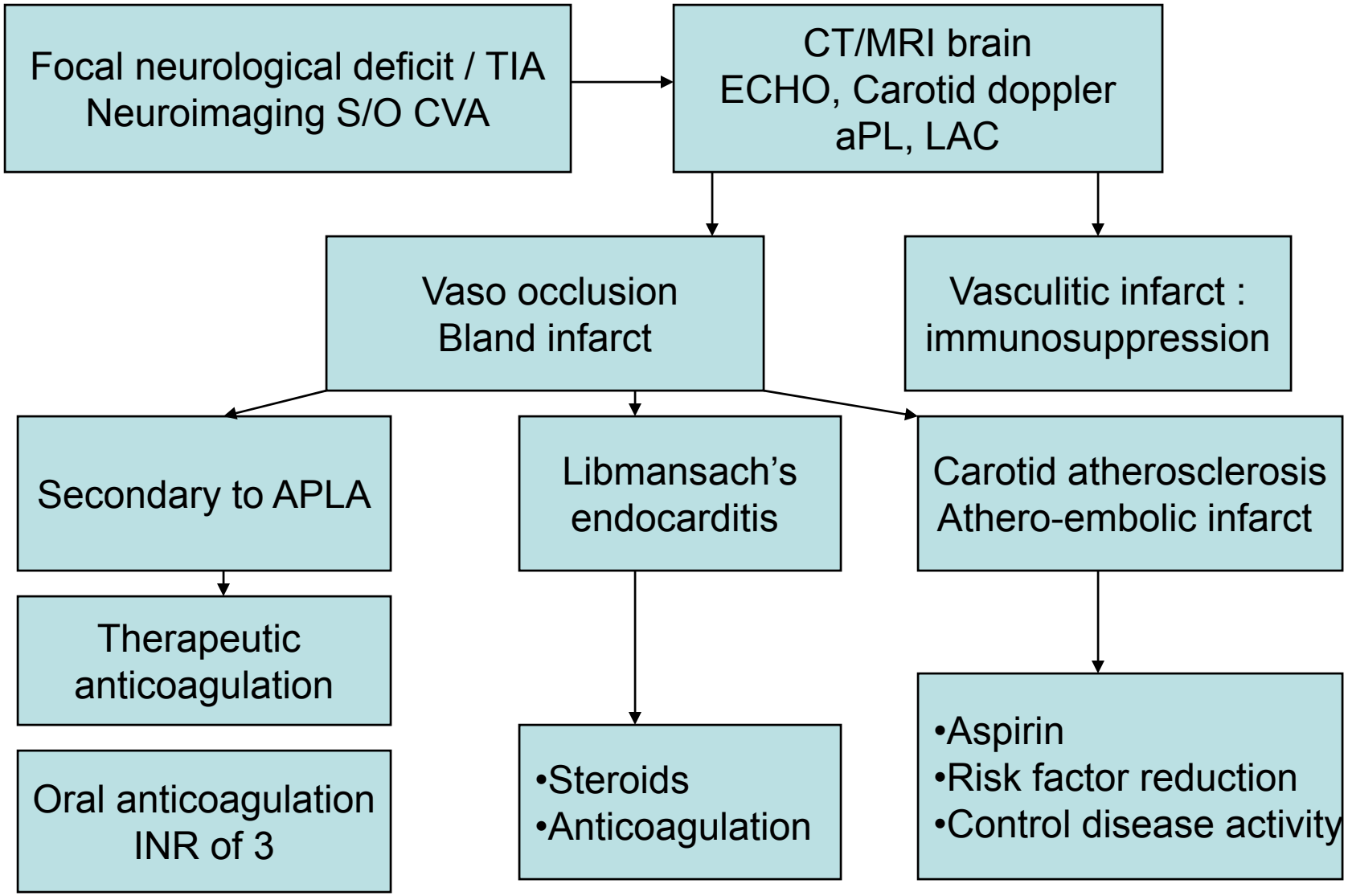
Slobodin G. Emerg Med J.2006;23(9):667-71

Neurological emergencies

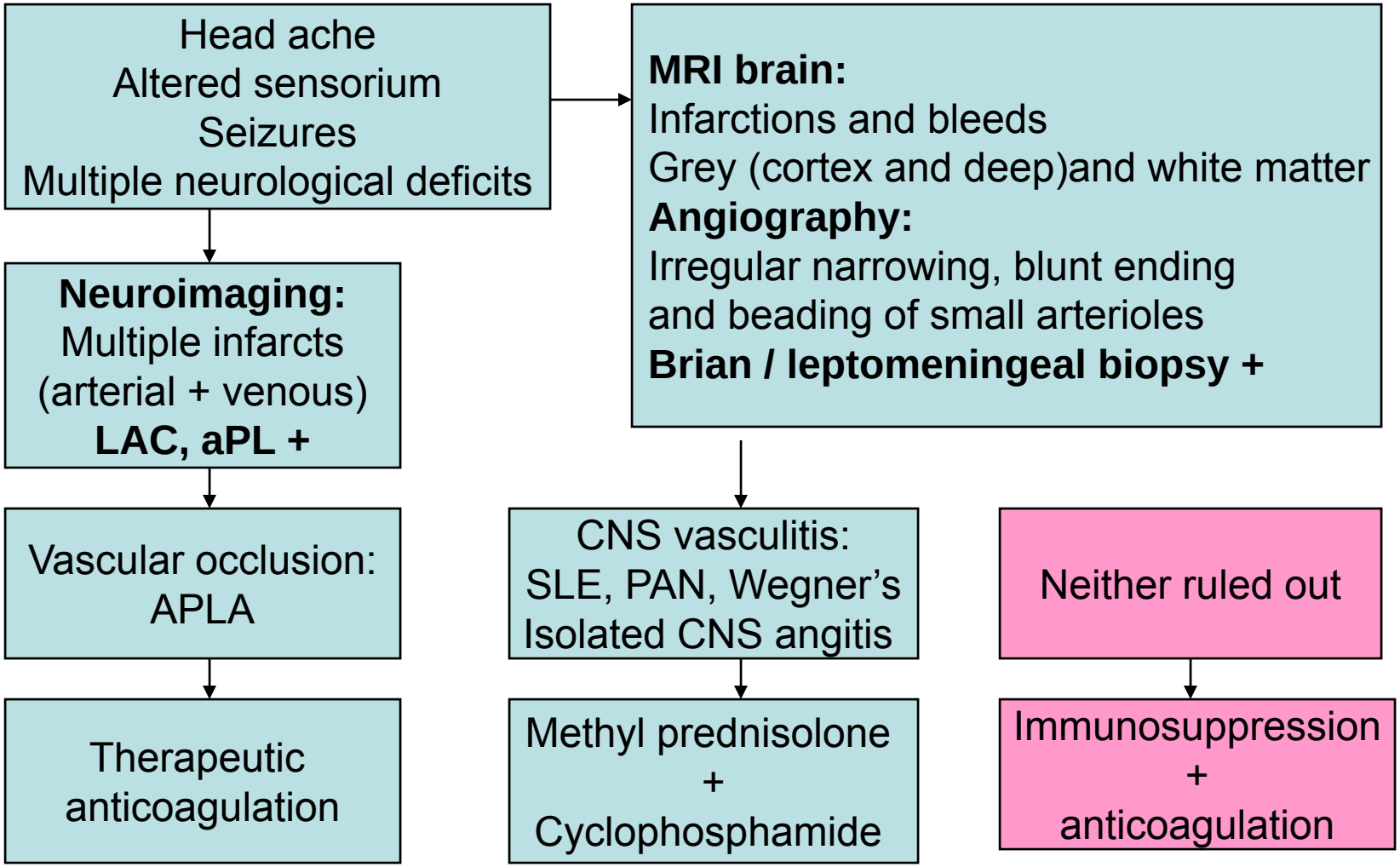
Meningitis


Acute onset illness;
Fever, head ache, signs of meningeal irritation
CSF Analysis
Neutrophilic pleocytosis
Elevated protein
Low glucose levels
Gram stain and CSF culture +
Lymphocytic pleocytosis
Normal/mild elevation of protein
Normal sugar levels
Gram stain and CSF culture -
Bacterial meningitis :
Empirical antibiotics
Ceftrioxone + Vancomycin
+ Ampicillin
Aseptic meningitis
Steroids
Active disease:
SLE
Behcet's
Vasculitides
Treatment related:
•NSAIDS, IVIG induced
•Self limiting illness

Stroke (CVA)


Focal neurological deficit / TIA
Neuroimaging S/O CVA
CT/MRI brain
ECHO, Carotid doppler
aPL, LAC
Vaso occlusion
Bland infarct
Vasculitic infarct :
immunosuppression
Secondary to APLA
Libmansach's
endocarditis
Carotid atherosclerosis
Athero-embolic infarct
Therapeutic
anticoagulation
Oral anticoagulation
INR of 3
•Steroids
•Anticoagulation
•Aspirin
•Risk factor reduction
•Control disease activity

CNS vasculitis / diffuse vascular occlusion



Seizures

- In SLE and primary CNS angitis seizures are reported in upto 10% patients and in APLA, Wegner's granulomatosis to a lesser extent (2-3%)
- Multiple etiologies: post CVA, uremia, meningitis, disease activity

Treatment:

- Remove metabolic cause
- Seizures due to disease activity might respond to steroids alone
- Recurrent seizures respond to common antiepileptic drugs and long term treatment is not necessary

Other causes of altered sensorium include malignant hypertension, TTP, steroid induced psychosis, uremic encephalopathy

Hematologic emergencies

TTP in SLE

- Typical features of CNS, renal dysfunction, thrombocytopenia, anemia, schistocytes in PBS
- Mimics disease flare sometimes
- Plasma exchange is treatment of choice

Musio F. Semin Arthritis Rheum. 1998 ;28(1):1-19

- Plasma exchange daily sessions to be given till platelet count is >50,000/cc for 2 consecutive days
- Poor response to immunosuppressants when used alone

  steroids and CYC used as adjunctive therapy
- Relapses are common

Scleroderma crisis and catastrophic APLA mimic TTP

Hematological emergencies

Syndrome	Investigations	Treatment options
Autoimmune hemolytic anemia (warm antibody) (SLE)	PBS Hemolytic W/U Coombs test Serum LDH	High dose steroids IVIG (less effective) Splenectomy Rituximab ?
Autoimmune thrombocytopenia (SLE, APLA)	ANA aCL LAC	High dose steroids IVIG (0.4 g/kg/d for 5days) Rituximab (refractory cases) Splenectomy (refractory cases)

Autoimmune cytopenias - treatment

- IVIG administered alone or with steroids no benefit in terms of response rates or time to clinical response in thrombocytopenia

Jacobs P. Am J Med. 1994;97(1):55-9

- Rituximab (chimeric anti CD 20 antibody) has been used for refractory autoimmune hemolytic anemia* and thrombocytopenia^ with good response

**Perotta S. Br J Haematol. 2002 Feb;116(2):465-7*

^Lehembre S. Ann Dermatol Venereol. 2006 Jan;133(1):53-5

Cardiac emergencies

Cardiac ischemia

Disease	Pathology	Diagnosis	Treatment
SLE RA	Accelerated atherosclerosis	•Clinical •Immunological markers	•MX of ACS •Risk factor control •Disease activity control
PAN Churg-Strauss syndrome	Arteritis	•Clinical •Angiogram- aneurysm •HBS Ag / P-ANCA	•MX of ACS •Steroids + CYC
APLA	Thrombosis	•Clinical •LAC/ aCL	•MX of ACS •Lifelong anticoagulation
Takaysu arteritis	Arteritis	•Clinical features •Angiogram- stenosis, occlusion Post-stenotic dilatation, aneurysms	•MX of ACS •Steroids •Revascularization (After control of inflammation)

Arrhythmias

- Transient atrial fibrillation, flutter or PSVT in 20–30% of SSc patients
- NSVT was described in 7–13%
- SCD is reported in 5–21% SSc patients
- Management of AF, SVT, VT do not differ from patients without SSc

Seferovic PM. Rheumatology 2006;45:iv39–iv42

Myocarditis with CHF

- SLE presenting with CHF is rare with few case reports and case series
- Associated with nephritis (60%), and elevated anti-ds DNA antibodies (80%)
- Responsive to high dose steroids and supportive care
- Refractory cases require cyclophosphamide and IVIG

Chung JW. Rheumatol Int. 2008 28(3):275-80

- Case report of utility of immunoadsorption onto staphylococcal protein A

Griveas I. Ther Apher Dial. 2004;8:281-5

Pericardial tamponade

- Pericardial involvement is common in SLE (30-35%).

- Pericardial tamponade is uncommon and SLE contributes to 3.2% of all cases.
- Frequently associated with nephritis, Libman-Sacks endocarditis and myocarditis.

- Responds well to oral steroids and pericardial drainage
- Does not lead to constrictive pericarditis

Weich HS. Lupus. 2005;14(6):450-7

Pulmonary emergencies

Pulmonary embolism

- DVT/ PE are seen in patients with APLA

  8% of patients with APLA develop thrombotic events during 5 yr follow up

  Tarr T. Clin Rev Allergy Immunolo. 2007;32:131-7

  Strong association between LA and VTE (odds ratio, 9.4; 95% confidence interval [CI], 2.1 to 46.2)

  Jinsberg JS. Blood. 1995 Nov 15;86(10):3685-91.

- Initial evaluation and management does not differ from other cases of PE

  LAC cannot be tested in patients receiving heparin

- Patients with APLA, presenting with PE requires life long anticoagulation (INR - 3)

Ventilatory failure

- Acute or acute on chronic ventilatory failure can be seen in PM/DM
- High dose coticosteroids / pulse methyl prednisolone with methotrexate* and in refractory cases with IV Ig^ have been successfully used

**Haskard DO. Ann Rheum Dis. 1983 Aug;42(4):460-1*

**Obón Azuara B. An Med Interna. 2005 Sep;22(9):434-6*

^Daurait G. Eur J Intern Med. 2002 May;13(3):203-205

- NIV can be tried (level C evidence)

BTS guidelines. Thorax 2002;57:192–211

- IVIG is less effective in PM
- Plasmapheresis ineffective in both the conditions

Diffuse parenchymal lung disease

- Severe pneumonia
- Acute pneumonitis with DAD. Eg: SLE, PM/DM
- Diffuse alveolar hemorrhage
- Eosinophilic pneumonia. Eg: Churg-Strauss syndrome
- Drug induced. Eg: Methotrexate induced DPLD
  Sulfasalizine induced DAH
- Cardiogenic pulmonary edema due to myocarditis
- Fluid over due to oliguric ARF
- Uremic lung

Differentiation of DPLD

	Clinical features	Radiological features	BAL	Lung biopsy
Pneumonia	AHRF	Multilobar consolidation	Microbiological stains and Culture +	
Lupus pneumonitis	AHRF	Multilobar consolidation (lower lobes)		•DAD, NSIP •Org. pneum. •Capilliritis
DAH	•AHRF •Hemoptysis •Fall in Hb	Multilobar consolidation MRI:↑ signal in T2W image	•Hemorrhagic •Hemosiderin laden macroph.	•Capillaritis+/- •Hemosiderin macrophages
MTX induced DPLD	•h/o MTX	Diffuse interstitial pattern	Lymphocytosis High CD4:CD8	Desquamative lesions

Lupus pneumonitis

- 2-4% of patients with SLE, but it is presenting manifestation in 50% of them
- Histological picture shows predominant diffuse alveolar damage
- High dose steroids + broad spectrum ABx
- Steroid resistant cases might respond to CYC, IVIg, plasmapheresis, Rituximab*

**Lim SW. Intern Med J.2006;36:260-2*

**Van den Bergh B. Acta Clin Belg.2005;60(2):102-5*

- Mortality rates 50% once respiratory failure sets in

Methorexate induced DPLD

- Subacute to fulminant hypoxic respiratory failure
- Most cases (50%) develop during 1st 4 months of treatment with MTX
- Responds to withdrawal of MTX and early institution of steroids
- Mortality rate of 15-20%, up to 50% on re-challenge

Kremer JM. Arthritis Rheum 1997;40:1829–1837

Diffuse alveolar hemorrhage and Pulmonary renal syndromes

Disease	Renal	Arthritis	Skin vasculitis	ANA	C_L	Immun. markers	Tissue Ab. Staining
Wegner's granulomatosis	+	+	+	±	N	C-ANCA	–
Microscopic polyangitis	+	+	+	±	N	P-ANCA	–
Goodpasture's syndrome	+	–	–	–	N	Anti - GBM	Linear
SLE	+	+	±	+	↓	Anti ds-DNA	Granular
Isolated pulmonary capilliritis	–	–	–	–	N	–	

Isolated DAH reported in RA, PM/DM and MCTD
Pulmonary renal syndrome described in RA, SSc and MCTD

DAH - Treatment

SLE	Steroids + CYC	Plasmapheresis : used as salvage, no survival benefit (retrospective analysis) *Medicine.1997;76:192–202* Rituximab: anecdotal use *Nephrol Dial Transplant.2008;23(1):385-6* IVIg: anecdotal use
Wegner's granulomatosis & Microscopic polyangitis	Steroids + CYC	Plasmapheresis: useful (uncontroled study n=20) *Am J Kidney Dis 2003;42:1149–53* Rituximab: case reports *Intern Med. 2007;46(7):409-14*
Goodpasture's	Oral steroids + oral CYC + Plasmapheresis	
Unknown etiology	Steroids + CYC+ plasmapheresis	

Renal emergencies

RPGN

Disease	Lungs	Arthritis	Skin vasculitis	ANA	C_L	Immun. markers	Tissue Ab. Staining
Wegner's granulomatosis	+	+	+	±	N	C-ANCA	–
Microscopic polyangitis	+	+	+	±	N	P-ANCA	–
Goodpasture's syndrome	+	–	–	–	N	Anti - GBM	Linear
Anti GBM disease	–	–	–	–	N	Anti - GBM	Linear
SLE	+	+	±	+	↓	Anti ds-DNA	Granular
Renal limited crescentic GN	–	–	–	–	N	P-ANCA	–
Cryoglobulinemia	–	+	+	–	↓	Cryocrit Anti HCV	Granular

Malignant hypertension, scleroderma renal crisis and TTP are mimics

RPGN- Treatment

SLE	Steroids + CYC	Rituximab: case reports *Lupus. 2003;12(10):798-800* *Arthritis Rheum. 2007;56(4):1263-72* IVIg: useful as salvage (uncontroled study ,n=7) *Semin Arthritis Rheum. 2000 ;29(5):321-7*
Wegner's granulomatosis & Microscopic polyangitis	Steroids + CYC	Plasmapheresis: useful in cases requiring RRT *Ther Apher. 2001;5(3):176-81* Rituximab: useful in refractory cases (uncontroled study, n= 6*, 9^) **Arthritis Rheum 2005;52:262– 8* *^J Intern Med 2005;257:540– 8* IVIg: beneficial as single agent in wegner's (n=12) *Nephron Clin Pract. 2006;102(1):c35-42*
Goodpasture's	Oral steroids + oral CYC + Plasmapheresis	
Cryoglobulinemia	•IFNα+ ribavirin •Steroids+ CYC	Rituximab: useful in refractory cases retrospective analysis of 25 cases *J Nephrol. 2007 ;20(3):350-6*

Scleroderma renal crisis (SRC)

- **Accelerated hypertension and RPRF** occurring in a patient with systemic sclerosis
- CHF, arrhythmias, pericardial effusion (2° to HTn, renal failure)
- Upto 10% of patients with SSC develop SRC
- 10% of patients are apparently normotensive (eg: 95/60 to 145/80)

<u>Risk factors:</u>

Early disease (75% of cases develop in first 4 yrs of disease)

Diffuse SSC (25% patients develop SRC)

Renal hypoperfusion (sepsis, dehydration, drugs decreasing renal perfusion)

Steroid use (>40mg/day): Case control studies suggest increased risk

Steen VD. Arthritis Rheum 1998;41:1613– 9

Scleroderma renal crisis (SRC)

Factors that occur before onset of SRC that may be helpful in predicting SRC

Predictive of SRC	Not predictive of SRC
Diffuse skin involvement	Previous blood pressure elevation
Rapid progression of skin involvement	Abnormal urinalysis
Disease duration <4 years	Previous increase in serum creatinine
Anti-RNA polymerase III antibody	Anti-topoisomerase I (Scl-70) or anti-centromere antibodies
New anemia	Pathologic abnormalities in renal blood vessels
New cardiac events	
Pericardial effusion	
Congestive heart failure	
Antecedent high-dose corticosteroid	

Steen VD. Rheum Dis Clin N Am 29 (2003) 315–333

SRC – lab findings

Mild azotemia

- Might progress despite control of BP (peak level upto 3.8 mg/dl)
- Not attributed to ACE inhibhitors
- ACEI should not be discontinued for this reason

Microscopic hematuria

Proteinuria

Granular casts

Hemolytic anemia

Thrombocytopenia (rarely below 50,000/cc)

SRC- Treatment

Adequate control of blood pressure with ACE inhibitors (around 120/70)

Captopril is preferred (shorter half life and greater flexibility)

Addition of other agents (preferably ARBs) might be required for adequate control

SRC – treatment and prognosis

- Pre- captopril era <10% of patients survived the 1st year
  Current 5 yr survival rate is 65%.

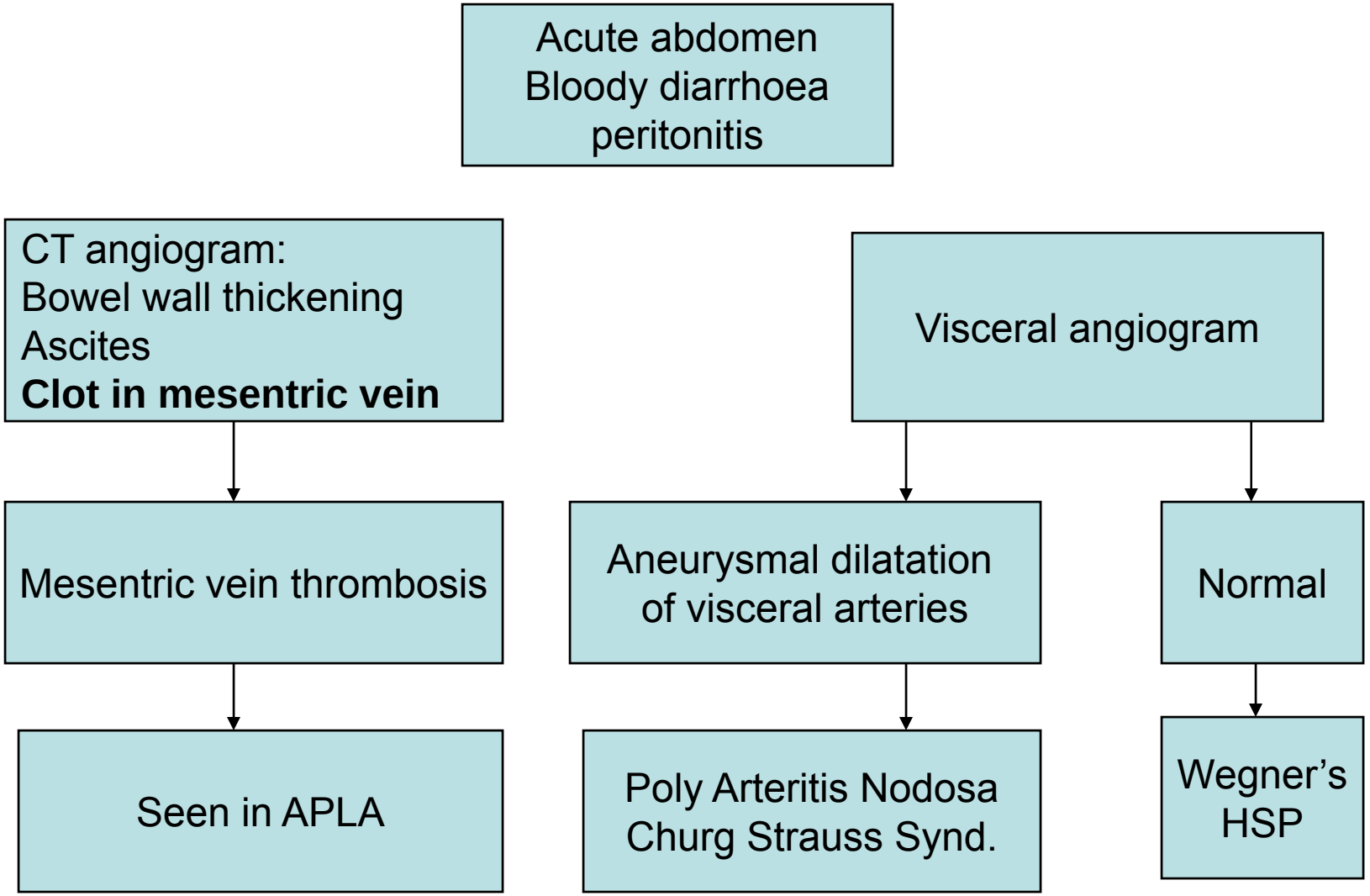
- Risk factors for bad outcome:
  Initial creatinine level >3 mg/dl
  Uncontrolled BP within 3 days
  Male gender, older age, presence of CHF

- 40% patients require long term RRT

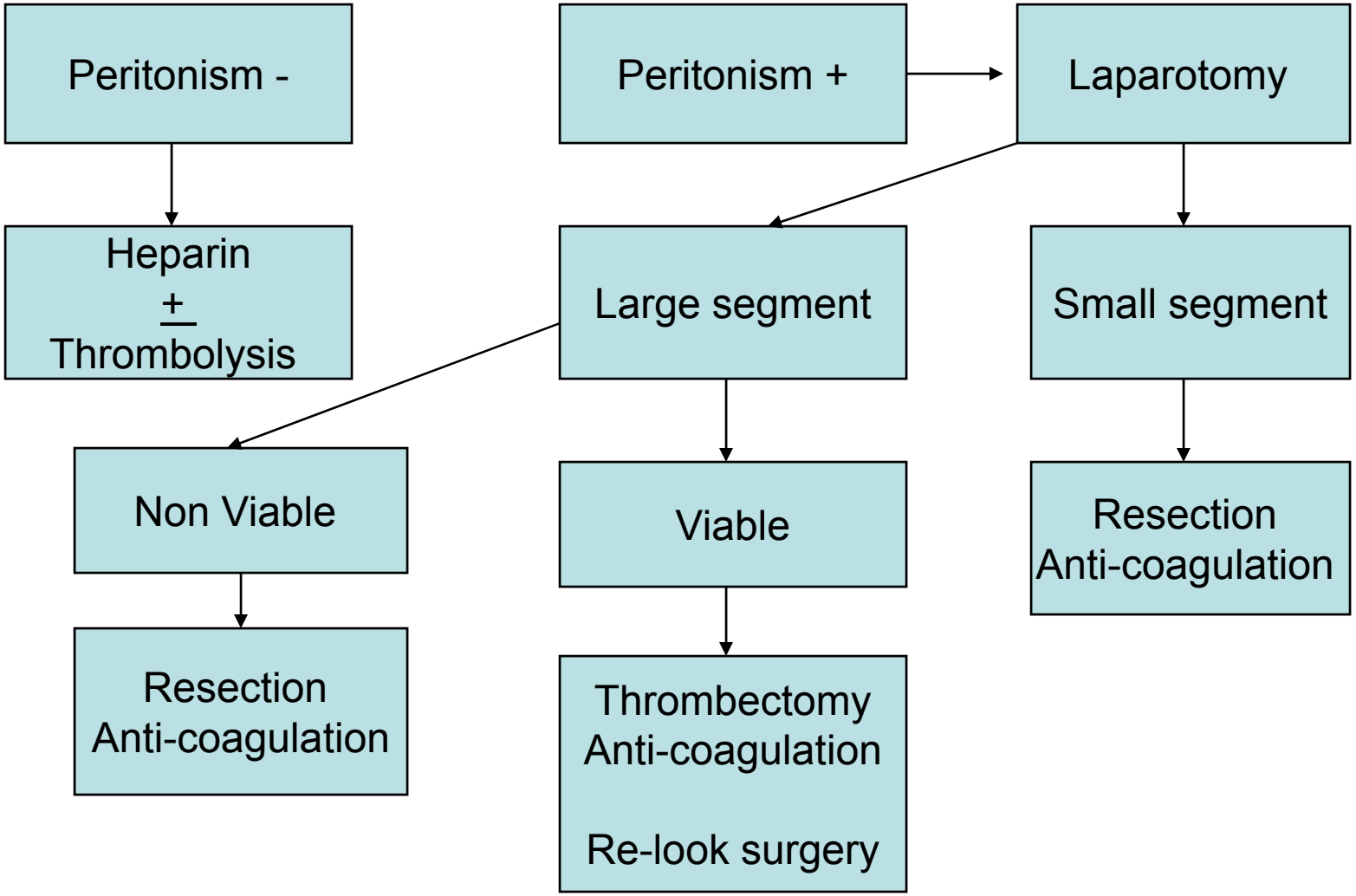
Steen VD. Ann Intern Med 2000;133:600– 3

Abdominal emergencies

Mesenteric ischemia



Mesenteric vein thrombosis



Visceral vasculitis

- PAN
- HSP
- Churg – Strauss Synd.
- RA
- Wegners granulomatosis

- Rarely : SLE, SSc, PM/DM, giant cell arteritis

- Acute abdomen with bloody diarrhoea
- Bowel infarction
- GI bleed
- Bowel perforation
- Cholecystitis
- Pancreatitis
- Appendicitis

Visceral vasculitis - management

Disease	Diagnosis	Treatment
PAN	•Clinical features •Visceral angiography: anurysmal dilatation •P- ANCA + rarely •HBS Ag + (50%)	Steroids +/-CYC Lamivudine/IFN γ
HSP	•Clinical features	Steroids
Wegner's granulomatosis	•Clinical features •C-ANCA +	Steroids +CYC
CSS	•Clinical features •Visceral angiography: anurysmal dilatation •P- ANCA +	Steroids+/- CYC
RA	•Clinical features •SC nodules, RF+	Steroids

Catastrophic APLA

- Seen in 1% of cases of APLA

- Multiple thromboses of medium and small **arteries** developing over a period of days
- Stroke, cardiac, hepatic, renal, adrenal, intestinal infarction and peripheral gangrene
- May present with adrenal insufficiency, but renal insufficiency uncommon (unlike TTP)

- aPL, LAC + (not seen in other mimics)

  Thrombocytopenia is usually present

  RBCs not fragmented (r/o TTP) and FDP not elevated (r/o DIC)

Catastrophic APLA

Diagnostic criteria:

1. 3 organ/ system involvement
2. Simultaneous/ within a week
3. HPE: small vessel occlusion
4. LAC/ aCL + twice 6 wks apart

Definitive : all 4 criteria

Probable:

criteria 1,2,4

criteria 1,3,4

All criteria but 2 organ involvement

All criteria but LAC/ aCL tested once

Treatment:

Anticoagulation
+
Steroids
+
PE or IVIG

} 70% success

Cause of death : CNS, cardiac involvement and infection

Buciarelii S. Arthritis Rheum. 2006;54(8):2568-76
Asherson RA. Medicine (Baltimore).1998;77(3):195-207

Summary

- Rheumatic diseases can present with protean manifestation involving any organ system
- High index of suspicion in a given clinical setting and appropriate investigations help in early diagnosis
- Current therapeutic modalities (immunosuppression, plasmapheresis, IVIg) give good results when initiated in time
- Newer therapeutic modalities like Rituximab is being explored as salvage therapy in various clinical settings with good results

Thank you