CRACKCast Episode 118 – SLE and Vasculitides

Episode Overview:

1. What the pathophysiology of lupus
2. List diagnostic criteria for SLE
3. List drugs that induce lupus
4. Describe the clinical manifestations w/ classic triad & symptoms and signs by system in lupus
5. List 3 drug regimens to treat SLE
6. How does neonatal lupus present?
7. What is antiphospholipid syndrome? What is the unusual laboratory feature seen with this condition?
8. What is the pathophysiology of vasculitis?
9. Give examples of:
    a. Large vessel vasculitis
    b. Medium vessel vasculitis
    c. Small vessel vasculitis
    d. Hypersensitivity vasculitis
    e. Subcutaneous vasculitis
10. Compare the findings for vasculitis
11. List 5 criteria for dx of temporal arteritis + 2 associated features
12. Describe the features of Behcet's Disease
13. List 10 causes of Erythema Nodosum
14. Compare Buerger's, Serum sickness and Hypersensitivity Vasculitis
15. List the diagnosis Criteria for HSP

Wise-Cracks

1. What is the differential for SLE patient and Chest pain?
2. Name and identify 2 pathognomonic clinical features for lupus
3. When should Rheum be involved in the ED with a SLE patient?
4. Spot Diagnosis: A 36-year-old female stock trader present with what appears to be necrosis of the nose and ears…
5. Spot diagnosis: 13 year old presents with abdo pain, polyarticular arthritis, foaming urine and the following rash…
6. Rounds Pimper: List 10 side effects of chronic steroid use

Rosens in Perspective

Systemic Lupus Erythematosus (SLE)

- SLE may affect any organ system. Thus, a fundamental understanding of the disease is required to tailor the differential diagnosis and evaluation.
- A 50-fold increased risk of coronary artery disease (CAD) and up to a 30-fold increased risk of venous thromboembolism in patients with SLE prompt chest pain evaluations in the emergency department (ED), even in young women.
- An elevated C-reactive protein level is more closely linked to infection in SLE patients and is not reflective of SLE disease activity
- An isolated elevated partial thromboplastin time (PTT) in a patient with SLE prompts consideration for antiphospholipid (aPL) antibody carrier state and, if there is a history of thrombosis, antiphospholipid syndrome (APS).
- Steroids are the mainstay for management of the majority of conditions that are associated with increased SLE disease activity, including musculoskeletal, cutaneous, renal, pleural, and pericardial disease.

- APS is common in patients with SLE and carries with it a risk of venous (typically deep venous thrombosis or pulmonary embolism) and arterial (most commonly stroke) thrombosis.
- Consultation with a rheumatologist may be helpful in diagnostic, management, and disposition decisions for patients with SLE.

Vasculitides

- Vasculitis syndromes should be considered in the presence of systemic symptoms, such as fever, malaise, and weight loss plus pulmonary, renal, or cutaneous manifestations.
- Massive hemoptysis and acute renal failure can occur in Wegener's granulomatosis, Goodpasture's disease, microscopic polyangiitis, and Churg-Strauss syndrome.
- Tracheal stenosis may be present in Wegener's granulomatosis, further complicating airway management.
- Many patients with established vasculitis are receiving high-dose or combination immunosuppressive therapy, making them vulnerable to opportunistic infections and overwhelming sepsis.

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[1] What the pathophysiology of lupus?

If you don't know, it's because no one truly knows!!! This is a *multisystem autoimmune disease* with every clinical manifestation known to man!

- 90% cases are women = strong role of **estrogen**? Throw on top of that importance of HLA alleles giving lots of overlap, making **genetics** a strong risk factor.
- SLE is the "prototype of all systemic autoimmune disease." Long story short, the body starts producing antibodies via B-Cells directed towards host antigens, IE starts attacking itself.
- These auto-antibodies (think for example anti– double-stranded DNA antibody) start destroying multiple organ systems

[2] List diagnostic criteria for SLE

- See table 108.1 in Rosens 9th Edition – SLE and Vasculitides

Clinical Criteria	Immunological Criteria
• Acute cutaneous lupus • Chronic cutaneous lupus • Oral ulcers • Non-scarring alopecia • Synovitis • Serositis • Renal disorder • Neurological disorder • Hemolytic anemia / leukopenia / thrombocytopenia	• ANA elevation • Anti-Sm elevation • aPL antibody elevation • Low complement levels • Direct coombs test positive

Table 108.1 is very busy
Remember the only mnemonic from med school

SOAP BRAIN MD

Serositis
Oral Ulcers
Arthritis
Photosensitivity & Pulmonary Fibrosis

Blood cells (pancytopenia)
Renal, Raynauds
ANA
Immunologic (anti-Sm, anti-dsDNA)
Neuropsych

Malar Rash
Discoid Rash

[3] List drugs that induce lupus

- See Box 108.2 from Rosens 8th Edition – SLE and Vasculitides

Drugs Definitively Implicated in Causing Drug-Induced Lupus

- Procainamide
- Hydralazine
- Methyldopa
- Chlorpromazine
- Isoniazid
- Quinidine
- Minocycline

[4] Describe the clinical manifestations of SLE with classic triad & symptoms and signs by system

In general, 4 broad presentations

1. Symptoms related to SLE that is not yet diagnosed (eg. idiopathic pericarditis, new rash)
2. Progression or acute deterioration due to known SLE (eg, progressive nephritis, lupus enteritis)
3. Complications of immunosuppression from treatment of SLE (eg, opportunistic infection)
4. Complaints or disease unrelated to SLE (eg. trauma, pregnancy).

See Table 108.3 in Rosen's 9th Edition – SLE and Vasculitides Chapter

Common or specific differential considerations with patients with SLE based on common presentations, comorbidities, or complications

Pleuritic Chest Pain	Pericarditis, pleuritic, PE, PNA, MSK chest wall pain
Delirium	Neuropsychiatric lupus, steroid psychosis
Leg Swelling	DVT, renal failure, right heart failure, protein losing enteropathy
Shortness of breath	PNA, anemia, pericarditis +/- effusion, pleuritic +/- effusion, ILD, shrinking lung syndrome
Pruritic or painful rash	Discoid SLE, drug reaction, sun exposure
Abdominal pain	Lupus enteritis, PUD, pancreatitis, pseudoobstruction
Fever	Infection, increased disease activity
Arthritis	Arthralgias, OA, septic arthritis, unrelated (gout, fibromyalgia)

[5] List 3 drug regimens to treat SLE

- **See table 108.4** in Rosen's 9th Edition – SLE and Vasculitides

Medications and typical dosing range for acute SLE exacerbations

Medication	Medication Class	Typical Regimen
Methylprednisolone	Glucocorticoid	1-2mg/kg IV once daily
Prednisone	Glucocorticoid	1-2mg/kg PO once daily
Hydroxychloroquine	Anti-malarial	200-400mg PO once daily
Cyclophosphamide	Alkylating agent	500-750mg/m^2 IV once
Azathioprine	Antimetabolite	25-50mg/day IV or PO

[6] How does neonatal lupus present?

1. Rash
    a. Erythematous annular lesions or arcuate macules with slight central atrophy and raised active margins look on scalp and face
    b. Can be confused with fungal infection, present at delivery or not until child has been exposed to UV
2. Heart Block
    a. From first degree to complete
3. Hepatic
    a. elevated liver enzymes
    b. mild hepatosplenomegaly
    c. Cholestasis
    d. hepatitis
4. Neurologic
    a. Hydrocephalus
    b. macrocephaly
5. Hematologic
    a. Anemia
    b. Neutropenia
    c. Thrombocytopenia
    d. aplastic anemia

[7] What is antiphospholipid syndrome? What is the unusual laboratory feature seen with this condition?

Nearly 40% of SLE patients have APS!!! Happens when auto-antibodies are directed towards serum proteins. Examples:

- ❑ Lupus anticoagulant: most thrombogenic
- ❑ Anticardiolipin antibody
- ❑ Anti–β2-glycoprotein I antibody.

Box 108.1 – Rosens 8th Edition – SLE Vasculitides

Common clinical features of antiphospholipid syndrome

- Venous thrombosis
- Arterial thrombosis including stroke and TIA
- Recurrent miscarriage
- Livedo reticularis
- Thrombocytopenia

Note: "A small subset of those with APS may present with multiple thrombotic sites and organ failures simultaneously. This condition is known as catastrophic APS."

Abnormal labs:

1. Elevated PTT in the setting of a normal PT/INR
    a. Due to interference of the coagulation study by aPL antibodies. Confirm w/ mixing study.
    b. "A mixing study requires repeating the PTT with a mixture of the patient's blood and a 50% contribution from normal, control serum. In the presence of an inhibiting antibody, the PTT will remain elevated. If, however, the PTT was elevated for other reasons (most commonly heparin), the addition of normal clotting factors from the control serum will restore the PTT to normal."
2. False positive VDRL
    a. "The Venereal Disease Research Laboratory (VDRL) assay to test for syphilis contains cardiolipin and thus will commonly be falsely positive in patients with anticardiolipin antibodies or APS."

[8] What is the pathophysiology of vasculitis?

Easy answer: unknown

As Rosen's states*: "The cause of most vasculitis syndromes is unknown. Most cases are believed to result from immune complex deposition in blood vessel walls, prompting a complement-mediated inflammatory reaction. This results in vessel wall damage and necrosis, leading to stenosis, occlusion, and subsequent end-organ ischemia. The clinical manifestations are determined predominantly by the size and distribution of blood vessels involved along with the histologic subtype of inflammation."*

[9] Give examples of vasculitides based on vessel size

See table 108.5 in Rosens 9th Edition – SLE and Vasculitides

a. Large vessel vasculitis
    i. Giant cell arteritis (GCA)
    ii. Takayasu's arteritis
b. Medium vessel vasculitis
    i. Polyarteritis nodosa
    ii. Buerger's disease
    iii. Kawasaki disease
c. Small vessel vasculitis
    i. Goodpasture's disease
    ii. Wegener's granulomatosis
    iii. Microscopic polyangiitis

iv. Churg-strauss
v. Behcet's disease
vi. HSP

d. Hypersensitivity vasculitis
e. Subcutaneous vasculitis

[10] Compare the findings for vasculitis

- See table 108.6 in Rosens 9th Edition – SLE and Vasculitides

Essentially Rosens breaks it down by the relative presence of a variety of clinical and investigative findings based on the type of vasculitis you are dealing with, including considerations for features like:

- Pulmonary infiltrates and nodules
- Alveolar hemorrhage
- Glomerulonephritis
- Upper airway disease
- Purpura
- Peripheral nervous system involvement
- Central nervous system involvement

[11] List 5 criteria for the diagnosis of temporal arteritis and two associated features

- See box 108.4 in Rosens 8th Edition – SLE and Vasculitides

American College of Rheumatology Classification Criteria for GCA

- Age over 50 years old
- New onset localized headache
- Temporal artery tenderness or decreased temporal artery pulse
- ESR >50mm/hr
- Abnormal arterial biopsy specimen characterized by mononuclear infiltration or granulomatous inflammation

Associated features:

- Vision loss
- Jaw claudication

[12] Describe the features of Behcet's Disease

Behçet's disease = complex, chronic small-vessel vasculitis that may affect:

- ❑ Mucocutaneous
- ❑ Ocular
- ❑ Cardiovascular
- ❑ Renal
- ❑ Gastrointestinal
- ❑ Pulmonary
- ❑ Urologic
- ❑ Musculoskeletal
- ❑ central nervous systems.

The ancient Greeks knew about it!

Definition includes the presence of:

- Aphthous oral ulcers
- Plus two or more of the following
    - Genital aphthae
    - Cutaneous lesions
    - Neurologic, oral, or rheumatologic manifestations

Classic triad for Behçet's disease

1. Oral aphthous ulcers
2. Genital ulcers
3. Uveitis

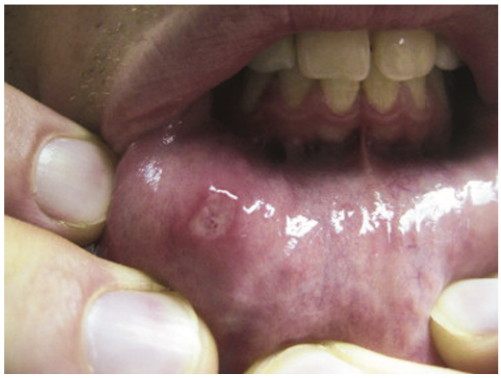


Fig. 108.9. Oral aphthae associated with Behçet's disease. (From Firestein GS: Kelley's textbook of rheumatology, ed 8, Philadelphia, 2008, WB Saunders.)

[13] List 10 causes of Erythema Nodosum

1. Viral upper respiratory tract infections
2. Streptococcal infection
3. Tuberculosis
4. Sarcoidosis
5. Penicillins
6. Sulfonamides
7. Oral contraceptive medication
8. Phenytoin
9. IBD
10. SLE
11. Histoplasmosis
12. Yersinia
13. Salmonella
14. Chlamydia infections
15. Coccidioidomycosis
16. Psittacosis (parrot fever)

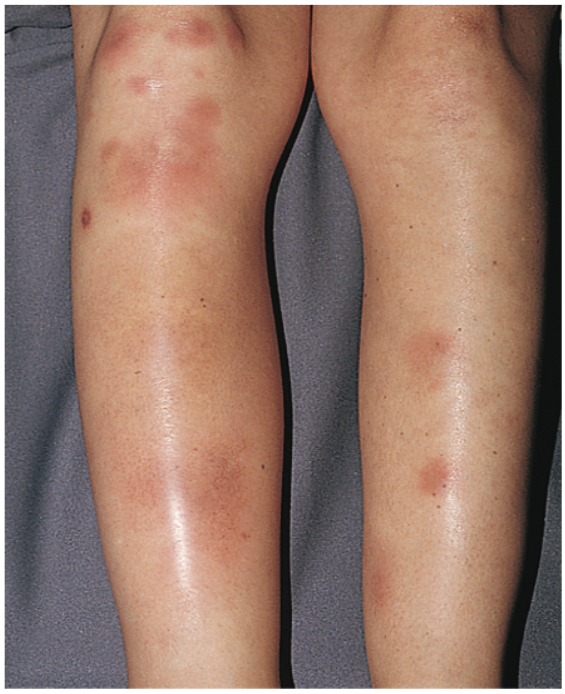


Fig. 108.7. Tender subcutaneous nodules associated with erythema nodosum. (From Kliegman R: Nelson textbook of pediatrics, ed 18, Philadelphia, 2007, WB Saunders.)

[14] Compare Buerger's, serum sickness and hypersensitivity vasculitis

See Table 108.7 in Rosen's 9th Edition –SLE and Vasculitides

	BUERGERS DISEASE	SERUM SICKNESS	HYPERSENSITIVITY VASCULITIS
Pathophysiology	Small / medium arteries and veins of the extremities	Immune complex deposition in blood vessel walls	Small vessel
Associated exposures	Heavy cigarette smoking Cold exposure	Foreign protein or serum Penicillin based antimicrobials Sulfa drugs NSAIDs	Beta lactam abx NSAIDs Diuretics
Common symptoms	Pain, paresthesias, claudication, rest pain	Fever, arthralgias, diffuse lymphadenopathy. Pruritic skin lesions	Typically confined to skin (vs. serum sickness)
Physical exam findings	Poorly healing wounds Ulcerations Splinter hemorrhages Digital ischemia and necrosis Distal to proximal progression	Urticaria Purpuric skin lesions Scarlatiniform rash Erythema multiforme Azotemia, proteinuria Myocarditis, pericarditis	Palpable purpura in dependent regions including legs and buttocks Urticarial vasculitis Livedo reticularis Skin nodules and ulcers
Diagnosis	Angiography: demonstrates Corkscrew pattern of collateral vessels – rule out other ischemia causes	Clinical	Clinical
Management and outcome	Smoking cessation Meticulous wound care Protection from trauma and thermal injury	Supportive Systemic steroids if severe Recovery generally 4-6 weeks	Supportive Systemic steroids if severe

[15] List the diagnostic criteria for HSP

2 or more of the following:

- ❏ Age < 20
- ❏ Palpable Purpura
- ❏ Abdominal pain
- ❏ Vessel wall granulocytes on biopsy

Wise Cracks

[1] What is the differential for SLE patient and Chest pain?

See Table 108.2 Rosens 9th Edition – SLE and Vasculitides

- Pleuritis
- Pulmonary embolism
- Pneumonia
- Pericarditis
- Coronary artery disease

[2] Name and identify 2 pathognomonic clinical features for lupus

Malar Rash & Discoid Lupus

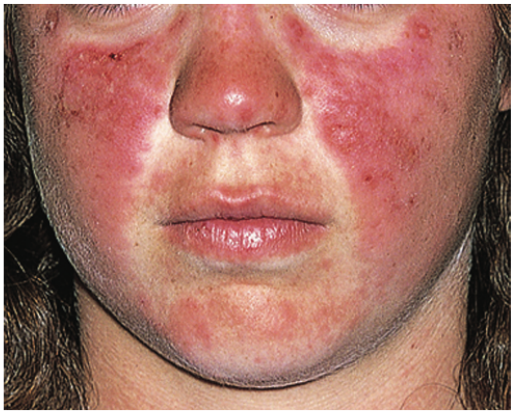


Fig. 108.4. The malar or butterfly rash is the hallmark of systemic lupus erythematosus (SLE). (From Habif TP: Clinical dermatology, ed 4, New York, 2004, Mosby, pp 592–606.)

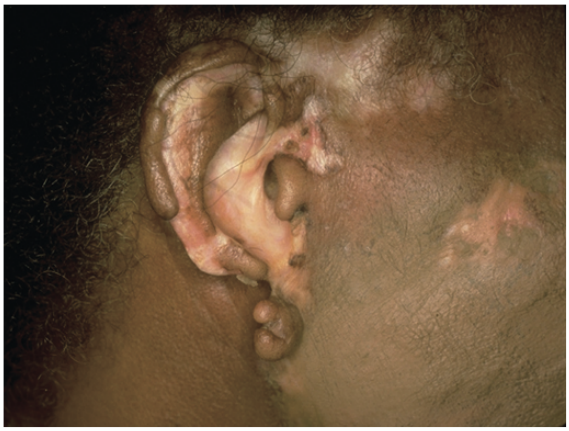


Fig. 108.5. Right ear of a patient suffering from chronic discoid lupus. Note pigment change and tissue destruction. (Courtesy Professor Gregory Raugi, University of Washington.)

[3] When should rheumatology be involved in the ED with a SLE patient?

Hold up - your SLE patient is not just an automatic turf to CTU! Here is an important list to consider from box 108.3 in Rosens 8th Edition – SLE and Vasculitides

Reasons for rheumatological referral for patients with SLE

- To confirm a diagnosis
- To assess disease activity and severity
- To provide general disease management
- To manage uncontrolled disease
- To manage organ involvement or life-threatening disease
- To manage or prevent treatment toxicities
- Special circumstances (APS, pregnancy, surgery)

[4] Spot Diagnosis: A 36 year old female stock trader present with what appears to be necrosis of the nose and ears…

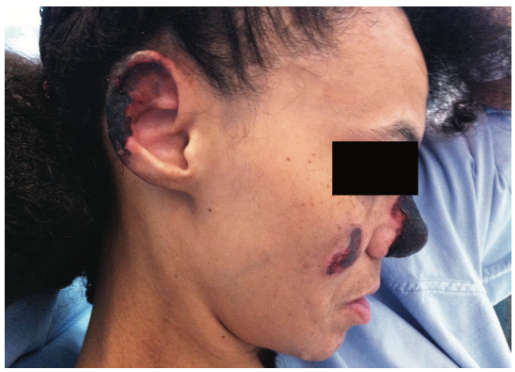


Fig. 108.10. Vasculitic lesions caused by crack cocaine containing levamisole. (Courtesy Dr. Christopher Hicks, University of Toronto.)

[5] Spot diagnosis: 13 year old presents with abdo pain, polyarticular arthritis, foaming urine and the following rash...

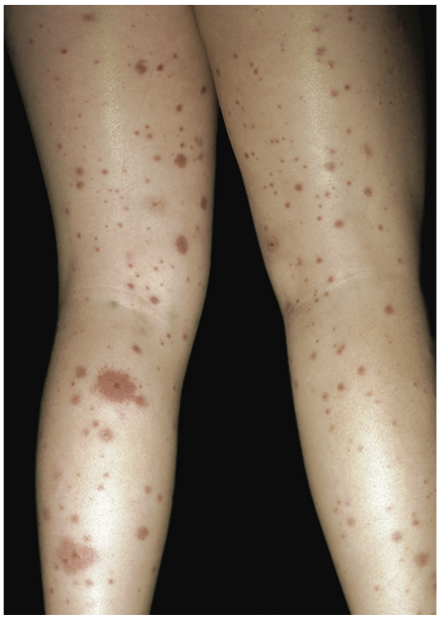
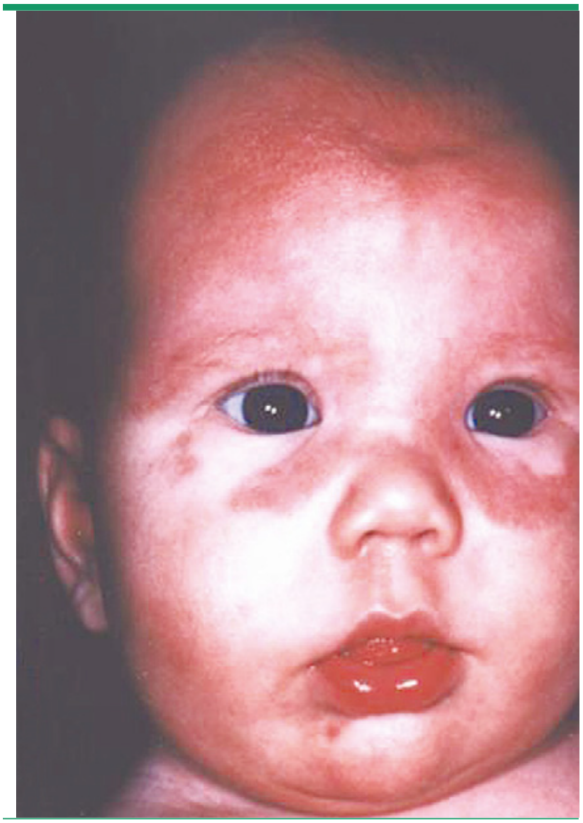


Fig. 108.8. Purpuric lesions associated with Henoch-Schönlein purpura, some of which have coalesced and undergone central necrosis. (From Habif TP: Clinical dermatology, ed 5, New York, 2009, Mosby.)

Neonate 1 week post delivery

Neonatal lupus rash



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[6] Rounds Pimper: List 10 side effects of chronic steroid use

1. Psychosis
2. Amenorrhea
3. Moon Facies
4. Obesity
5. Buffalo Hump
6. Striae
7. Poor wound healing / ulcers
8. Muscle weakness
9. Osteoporosis
10. Avascular necrosis
11. Immunosuppression & recurrent infections
12. Hyperglycemia
13. Hypertension