The Rheumatology Block

Rheumatoid arthritis, systemic lupus erythematosus, axial spondyloarthritis, vasculitis, crystal arthropathy and antiphospholipid syndrome.

Cases 58–63 · 8,021 words

This block covers the rheumatology teaching of both internal medicine courses. The **first course** supplies cases 58 and 60; the **second course** supplies cases 61 and 63.

Case	Lecture it serves
System opener: the rheumatological history and examination	History taking in rheumatology; physical examination in rheumatology
Case 58 — Rheumatoid arthritis	Rheumatoid arthritis
Case 59 — Systemic lupus erythematosus	Systemic lupus erythematosus
Case 60 — Axial spondyloarthritis	Spondyloarthritis
Case 61 — Vasculitis	Vasculitis syndromes
Case 62 — Gout and calcium pyrophosphate deposition disease	Gout and pseudogout
Case 63 — Antiphospholipid syndrome	Antiphospholipid antibody syndrome

The approach to the patient with polyarthritis, a second-course seminar, is covered as Seminar 6 in Part Two, where the differential can be built from the pattern of joint involvement rather than from a named disease.

System Opener · The Rheumatological History and Examination

Almost every rheumatological diagnosis is reached through three questions asked in order: **is the pain inflammatory or mechanical; what is the pattern of joint involvement; and what is happening outside the joints.** Get those three right and the serology usually confirms what you already suspect.

Question 1 — Inflammatory or mechanical?

	Inflammatory	Mechanical
Morning stiffness	More than 30–60 minutes	Under 30 minutes
Effect of activity	Improves with movement	Worsens with use
Effect of rest	Worsens — stiffness after sitting	Improves
Night pain	Wakes the patient, typically in the second half of the night	Uncommon, and related to position
Swelling	Soft tissue swelling, warmth, effusion	Bony swelling only, or none
Systemic features	Fatigue, fever, weight loss	Absent

Question 2 — What is the pattern?

- **Number:** monoarthritis, oligoarthritis (four or fewer joints), or polyarthritis (five or more).
- **Symmetry:** symmetrical in rheumatoid arthritis and lupus; asymmetrical in the spondyloarthritides and gout.
- **Size and distribution:** small joints of the hands with **metacarpophalangeal and proximal interphalangeal involvement sparing the distal interphalangeal joints** points to rheumatoid arthritis; **distal interphalangeal involvement** points to psoriatic arthritis or osteoarthritis.
- **Axial or peripheral**, and whether the course is additive, migratory or intermittent.
- **Duration:** an inflammatory arthritis of less than six weeks is often viral or reactive and may resolve; beyond six weeks it demands a diagnosis.

Question 3 — What is happening outside the joints?

This is the part of the history that separates rheumatology from orthopaedics, and it is where the diagnosis usually is.

System	Ask about
Skin and hair	Photosensitive or malar rash, psoriasis — and look at the scalp, natal cleft, umbilicus and nails, not only the elbows; nodules; ulcers; purpura; hair loss; Raynaud phenomenon
Eyes	Dry eyes, a painful red eye with photophobia (uveitis), scleritis, and any visual loss
Mouth and genitals	Oral ulcers — painless in lupus, painful and recurrent with genital ulceration in Behçet disease, which is not rare in this region
Chest	Pleuritic pain, breathlessness, dry cough (interstitial lung disease)
Gastrointestinal	Diarrhoea, blood or mucus, weight loss (inflammatory bowel disease); dysphagia
Genitourinary	Urethral discharge or dysuria, and any preceding gastrointestinal or genitourinary infection (reactive arthritis)
Neurological	Temporal headache and jaw claudication in a patient over 50; numbness or weakness suggesting entrapment or mononeuritis multiplex; seizures
Renal	Frothy urine, ankle swelling, hypertension — all of which are silent until asked about

RED FLAGS THAT OVERRIDE THE REST OF THE ASSESSMENT

A single hot, swollen, painful joint is septic arthritis until proved otherwise. Aspirate it, send it, and start antibiotics. A joint can be destroyed within days, and gout and sepsis coexist.

New severe back pain with neurological signs, fever, or a history of malignancy — image urgently.

New headache with jaw claudication or visual symptoms in a patient over 50 — giant cell arteritis; start corticosteroids immediately and arrange same-day assessment. Do not wait for the biopsy.

The examination

- **Screen with gait, arms, legs and spine**, then examine the affected regions in detail using **look, feel, move** followed by an assessment of function.
- **Recognise synovitis:** soft, boggy swelling with warmth and tenderness at the joint line, and an effusion. Distinguish it from the hard bony swelling of osteoarthritis — the treatment implications are entirely different.
- **Squeeze across the metacarpophalangeal and metatarsophalangeal rows.** Pain on the metatarsal squeeze is often the earliest sign of an inflammatory arthritis and is missed because feet are not examined.
- **Assess function, not just findings:** ask the patient to do up a button, hold a pen, lift a cup, and comb their hair. This tells you what the disease is actually costing them.
- **Then examine outside the joints** as the history directs — skin including hidden sites, nails, eyes, chest, abdomen, and the nervous system.

Case 58 · Rheumatoid Arthritis

CLINICAL VIGNETTE

A **42-year-old woman** describes five months of pain and swelling in the small joints of both hands, both wrists and the balls of both feet. She is **stiff for two hours every morning** and improves as the day goes on. She is exhausted, has difficulty with buttons, and can no longer open jars. She has cut back her working hours.

She smokes 10 cigarettes a day. Her mother had "bad arthritis".

On examination: symmetrical soft tissue swelling and tenderness of the metacarpophalangeal and proximal interphalangeal joints and both wrists, with **sparing of the distal interphalangeal joints**. The **metatarsophalangeal squeeze is painful bilaterally**. Grip strength is reduced. There are no nodules and no deformity yet.

Rheumatoid factor positive · anti-cyclic citrullinated peptide antibody strongly positive · C-reactive protein 48 · erythrocyte sedimentation rate 62. Radiographs: periarticular osteopenia with an early erosion at the fifth metatarsophalangeal joint.

THE WINDOW OF OPPORTUNITY

The damage in rheumatoid arthritis happens early, and it is permanent. Erosions appear within the first year, and function lost to established deformity is not recovered by later treatment.

Refer on suspicion, not on confirmation. A patient with persistent symmetrical small joint swelling should reach a rheumatologist within weeks, and disease-modifying therapy should begin within three months of symptom onset. Waiting for radiographic erosions or for a positive rheumatoid factor before referring is the single commonest and most costly error in this disease.

1. Focused History

- **Duration of morning stiffness in minutes**, pattern and symmetry of joint involvement, and which joints are spared.
- **Function** — dressing, grooming, cooking, work, driving. Record what she cannot do, not just what hurts.
- **Systemic features:** fatigue, low-grade fever, weight loss.
- **Extra-articular disease, asked about explicitly:** dry eyes and dry mouth; red painful eye; breathlessness and dry cough (interstitial lung disease); numbness in the hands (carpal tunnel) or asymmetric neuropathy (vasculitis); **neck pain and any arm or leg symptoms**, which raise cervical spine involvement.
- **Smoking** — it increases both the risk and the severity of the disease, reduces treatment response, and is the most important modifiable factor. Say so plainly to the patient.
- **Before immunosuppression:** pregnancy plans and contraception; infection history; **tuberculosis exposure and hepatitis B and C risk**; vaccination status.

2. Physical Examination

- Map the synovitis, counting tender and swollen joints. **Examine the feet** — metatarsophalangeal disease is frequently the earliest change.
- **Deformities of established disease**, which you should be able to name: ulnar deviation at the metacarpophalangeal joints, swan-neck and boutonnière deformities, Z-thumb, and a prominent piano-key ulnar head.

- **Rheumatoid nodules** over the extensor surfaces; carpal tunnel signs.

THE COMPLICATION THAT CATCHES SURGICAL TEAMS OUT

Ask about neck pain and examine the neurology in every patient with longstanding rheumatoid arthritis — particularly before any operation.

Erosion of the transverse ligament and the odontoid peg permits **atlantoaxial subluxation**. Neck extension during intubation can then cause cord compression. Imaging of the cervical spine before general anaesthesia is a standard precaution, and the anaesthetist must be told the diagnosis.

- **Extra-articular examination:** eyes for scleritis, episcleritis and dry eye; chest for fibrotic crackles and pleural effusion; heart for pericarditis; skin for vasculitic lesions and nailfold infarcts; abdomen for splenomegaly, which with neutropenia constitutes **Felty syndrome**.

3. Investigations

- **Rheumatoid factor and anti-cyclic citrullinated peptide antibody.** The latter is considerably more specific and predicts erosive disease. **Between a fifth and a third of patients are seronegative** — a negative result does not exclude the diagnosis in a patient with unmistakable synovitis.
- **C-reactive protein and erythrocyte sedimentation rate** for disease activity, and to follow response.
- Complete blood count — normocytic anaemia of chronic disease and reactive thrombocytosis; renal and liver function as a **baseline before disease-modifying drugs**.
- **Radiographs of hands and feet:** soft tissue swelling, periarticular osteopenia, uniform joint space narrowing, and **marginal erosions**. **Ultrasound or magnetic resonance imaging detects synovitis and erosions far earlier** and is increasingly used to confirm early disease.
- **Before biologic therapy: screen for latent tuberculosis** with an interferon-gamma release assay and chest radiograph, and for **hepatitis B and C** — including hepatitis B core antibody, because of the reactivation risk.

4. Management

Treat to a target

- Set an explicit target of **remission, or at minimum low disease activity**, measure it at each visit with a composite score, and **escalate therapy until the target is met**. Reviewing every one to three months in early disease is part of the treatment, not administrative overhead.

Drugs

Agent	Practical points
Methotrexate — first line	Weekly, never daily. Prescribe folic acid on a different day. Monitor complete blood count, liver and renal function. Contraindicated in pregnancy — effective contraception is required and it must be stopped well before conception. Avoid substantial alcohol. Caution with trimethoprim and co-trimoxazole, which are also antifolates.
Sulfasalazine, hydroxychloroquine, leflunomide	Used alone or in combination where methotrexate is not tolerated. Hydroxychloroquine requires annual retinal screening.
Bridging corticosteroids	Oral or intramuscular, or intra-articular injection, to control symptoms while the disease-modifying drug takes effect over 6–12 weeks. Use the lowest dose for the shortest time, with bone protection.
Biologic and targeted synthetic agents	Tumour necrosis factor inhibitors, rituximab, tocilizumab, abatacept, Janus kinase inhibitors, after inadequate response. Screen for tuberculosis and hepatitis first; vaccinate beforehand; and avoid live vaccines once immunosuppressed.
Anti-inflammatory drugs	For symptoms only — they modify nothing. Use with gastroprotection and with attention to renal and cardiovascular risk.

THE PRESCRIBING ERROR THAT KILLS

Methotrexate is dispensed as a **weekly** dose. Daily administration — through a prescribing error, a transcription error at admission, or a patient misunderstanding — causes fatal pancytopenia and mucositis, and it has happened repeatedly. **Confirm the day of the week with every patient at every visit, and check it on every drug chart you clerk.** Write the day on the prescription.

Beyond the prescription

- **Physiotherapy and occupational therapy** — hand exercises, joint protection, splinting, aids and workplace adaptation. **Smoking cessation.** Regular exercise and weight management.
- **Cardiovascular risk is substantially increased** by the disease itself, independently of traditional risk factors. Assess and treat it actively — this is a major cause of premature death in rheumatoid arthritis and is routinely neglected while attention stays on the joints.
- Osteoporosis assessment and prevention, particularly with corticosteroid exposure. Vaccination. Pregnancy planning with a compatible drug regimen.

5. Teaching Points and Viva Questions

- Refer on suspicion. The joints being destroyed while you wait for confirmation do not grow back.
- Squeeze the metatarsophalangeal joints — the feet declare the disease before the hands deform.
- Seronegative rheumatoid arthritis is common; the antibodies support the diagnosis, they do not make it.
- Methotrexate is weekly. Check it on every drug chart.
- Screen for tuberculosis and hepatitis B before any biologic agent.
- Image the cervical spine before anaesthesia, and tell the anaesthetist.

- Treat the cardiovascular risk as vigorously as the synovitis.

Questions you should be able to answer:

- Which features of this history tell you the arthritis is inflammatory?
- Her rheumatoid factor is negative. Does that change your management?
- She is listed for a hysterectomy. What must happen before she is anaesthetised?
- Name three things you must check before starting a tumour necrosis factor inhibitor.
- Why does she need her lipids and blood pressure checked in a rheumatology clinic?

Case 59 · Systemic Lupus Erythematosus

CLINICAL VIGNETTE

A **26-year-old woman** presents with four months of profound fatigue, aching and swelling of the small joints of both hands and both knees, and a rash across her cheeks that flares after she has been outdoors. She has recurrent **painless ulcers on the roof of her mouth**, and her hair has been coming out. For two weeks she has had sharp chest pain on deep inspiration. Over the past month she has noticed her urine is frothy and her ankles swell by evening.

On examination: an erythematous rash over both cheeks and the bridge of the nose **sparing the nasolabial folds**. Painless palatal ulcers. Synovitis of the metacarpophalangeal joints **without deformity or erosion**. A pleural rub at the left base. **Blood pressure 148/92 mmHg.** Pitting ankle oedema.

Haemoglobin 96 g/L · white cells 3.2 with lymphopenia · platelets 110 · antinuclear antibody 1:1280 · anti-double-stranded DNA strongly positive · C3 and C4 both low · creatinine 108 µmol/L · urine dipstick blood and protein · urine albumin-to-creatinine ratio 320 mg/mmol.

1. Focused History

Lupus is a multisystem disease and the history must be a systematic sweep. A patient who is asked only about their joints will have their nephritis found late.

System	Features to elicit
Constitutional	Fatigue — usually the dominant symptom and the one most often dismissed — fever, weight loss
Skin	Photosensitivity, malar rash sparing the nasolabial folds, discoid lesions that scar, alopecia, Raynaud phenomenon, livedo reticularis
Mucosal	Oral and nasal ulcers, characteristically painless and on the hard palate
Joints	Symmetrical small joint arthritis that is non-erosive; deformity, if present, is reducible
Serosal	Pleuritic chest pain, pericarditic pain relieved by sitting forward, breathlessness
Renal	Frothy urine, ankle swelling, hypertension — and none of these may be present, because lupus nephritis is silent until it is advanced
Neuropsychiatric	Seizures, psychosis, stroke, headache, cognitive impairment, mood disturbance
Haematological	Recurrent infection, bruising, and thrombosis
Obstetric	Recurrent miscarriage, fetal death, pre-eclampsia — which together with thrombosis raise the antiphospholipid syndrome

- **Drug history:** hydralazine, procainamide, isoniazid, minocycline and tumour necrosis factor inhibitors cause **drug-induced lupus**, which is anti-histone positive and characteristically **spares the kidneys and central nervous system** and resolves on withdrawal.
- Family history of autoimmune disease; and a careful infection history, since infection both mimics and complicates lupus.

2. Physical Examination

- **The rash:** the malar rash of lupus **spares the nasolabial folds**, which distinguishes it from rosacea and from dermatomyositis. Discoid lesions scar and cause permanent alopecia.
- Examine the **hard palate** for ulcers — patients do not report them because they do not hurt.

- Joints: synovitis without erosion; deformity, where present, is reducible (Jaccoud arthropathy).
- Chest and heart for rub and effusion; lymph nodes and spleen; a full neurological examination; digits for ischaemia and livedo.

THE TWO-MINUTE RULE

Measure the blood pressure and dipstick the urine at every single lupus consultation, in clinic and on the ward.

Lupus nephritis produces no symptoms until it produces renal failure. It is found by the dipstick or it is found too late. This costs thirty seconds and is the highest-yield thing you will do in the consultation.

3. Investigations

- **Antinuclear antibody is the screening test** — highly sensitive but poorly specific, and positive in many healthy people at low titre. **A negative antinuclear antibody makes lupus very unlikely.**
- **Anti-double-stranded DNA and anti-Smith antibodies are specific.** Anti-double-stranded DNA titre correlates with disease activity, particularly renal activity.
- **Complement C3 and C4 fall during active disease** as complement is consumed. With anti-double-stranded DNA, these are the two markers you follow over time.
- **Anti-Ro and anti-La** — essential before pregnancy, since they cross the placenta and cause **neonatal lupus and congenital complete heart block**. Anti-RNP in overlap syndromes.
- **Antiphospholipid antibodies** — lupus anticoagulant, anticardiolipin and anti-beta-2-glycoprotein I — **repeated at 12 weeks** to confirm persistence.

THE INFLAMMATORY MARKERS BEHAVE DIFFERENTLY HERE

The erythrocyte sedimentation rate rises with lupus activity. The C-reactive protein characteristically does not.

So in a febrile lupus patient, **a high C-reactive protein should make you think infection first**, not a flare — with serositis being the main lupus exception. This single distinction is one of the most useful in the whole disease, because these patients are immunosuppressed and infection is a leading cause of death.

- **Urinalysis with microscopy and a urine protein or albumin-to-creatinine ratio at every visit**; creatinine and estimated filtration rate.
- **Renal biopsy** where there is proteinuria, an active urinary sediment or unexplained renal impairment. It classifies the nephritis, and the class determines the treatment — this patient needs one.
- Complete blood count for the cytopenias; direct antiglobulin test; coagulation screen; imaging as directed.

4. Management

THE ONE DRUG EVERYBODY GETS

Hydroxychloroquine is given to essentially every patient with lupus, and continued indefinitely.

It reduces flares, reduces accrued organ damage, reduces thrombosis, and **improves survival**. It is safe in pregnancy and should be continued through it. Smoking reduces its effectiveness, which is one more reason to address it. Arrange **annual retinal screening**.

It is a cheap, well-tolerated drug that changes the natural history of the disease, and it is under-prescribed.

- **Sun protection and smoking cessation** for every patient.
- **Mild disease:** hydroxychloroquine, with short courses of anti-inflammatory drugs or low-dose corticosteroid for flares.
- **Moderate disease:** add methotrexate or azathioprine as a steroid-sparing agent.
- **Severe organ-threatening disease — nephritis, central nervous system involvement, severe cytopenias:** high-dose corticosteroid with **mycophenolate mofetil or cyclophosphamide** for induction, then maintenance immunosuppression. Biologic agents including belimumab, rituximab and anifrolumab are used as add-on therapy.
- **Minimising corticosteroid exposure is an explicit treatment goal.** A large share of the permanent damage accrued by lupus patients over a lifetime — bone, metabolic, cardiovascular, cataract, infection — comes from the steroids rather than from the disease.
- **Antiphospholipid syndrome:** anticoagulation after thrombosis; **direct oral anticoagulants are avoided in triple-positive and arterial disease**, where warfarin is used. Aspirin with low-molecular-weight heparin in pregnancy.

Pregnancy — plan it, do not react to it

- Conception should be planned during **at least six months of quiescent disease**, particularly after nephritis.
- **Continue hydroxychloroquine.** Azathioprine, tacrolimus and corticosteroids are compatible with pregnancy. **Mycophenolate, cyclophosphamide and methotrexate are teratogenic and must be stopped and substituted well in advance.**
- **Anti-Ro positivity requires fetal cardiac monitoring** for heart block. Aspirin reduces pre-eclampsia risk. Distinguishing pre-eclampsia from a renal flare in the third trimester is difficult and requires joint obstetric and rheumatological care.

Long-term

- Vaccination before immunosuppression; **accelerated atherosclerosis** means active cardiovascular risk management; bone protection; contraceptive advice, with caution over oestrogen in antiphospholipid syndrome; and vigilance for infection, which can look exactly like a flare.

5. Teaching Points and Viva Questions

- Blood pressure and urine dipstick every visit. Nephritis is silent.

- A high C-reactive protein in a febrile lupus patient means infection until proved otherwise.
- A negative antinuclear antibody essentially excludes lupus; a positive one proves very little on its own.
- Follow anti-double-stranded DNA and complement together to track activity.
- Hydroxychloroquine for everyone, forever.
- Much of the long-term damage is caused by steroids — spare them deliberately.
- Plan pregnancy in remission and change the teratogens beforehand.

Questions you should be able to answer:

- Which features of her rash favour lupus over rosacea?
- She is admitted febrile with a C-reactive protein of 180. Flare or infection?
- What does her renal biopsy add that the urine test does not?
- She wants to conceive next year. What are your steps over the next twelve months?
- Why do her complement levels fall when she is unwell?

Case 60 · Axial Spondyloarthritis

CLINICAL VIGNETTE

A **24-year-old man** has had low back and buttock pain for eighteen months. The buttock pain **alternates from side to side**. It wakes him at around four in the morning and he has to get up and move about; he is then **stiff for about ninety minutes**. The pain is better after football and worse after a day at a desk. He has been told he has mechanical back pain and has had two courses of physiotherapy for a disc problem.

He also has persistent right heel pain and a swollen second toe. Three months ago he had a painful red eye that was treated urgently at the eye hospital. His father has psoriasis.

On examination: loss of the normal lumbar lordosis. **Modified Schober test 3.5 cm** (normal is over 5 cm). **Chest expansion 3 cm.** Tenderness over both sacroiliac joints, tenderness at the Achilles insertion, and **dactylitis of the third toe**. Cervical rotation is reduced.

HLA-B27 positive · C-reactive protein 34. Radiographs show bilateral grade 3 sacroiliitis.

WHY THIS DIAGNOSIS IS MISSED FOR YEARS

The average delay between the onset of symptoms and the diagnosis of axial spondyloarthritis remains **several years**, and this patient shows why: a young man with back pain is assumed to have a mechanical problem, and is treated for it repeatedly.

The history distinguishes them completely, and it takes two minutes.

1. Inflammatory Back Pain

Four of the following five features indicate inflammatory back pain:

- **Age at onset below 45 years.**
- **Insidious onset**, present for more than three months.
- **Morning stiffness of more than 30 minutes.**
- **Improvement with exercise but not with rest.**
- **Night pain, particularly in the second half of the night, that improves on getting up.**

Alternating buttock pain is additionally characteristic and is worth asking about specifically. This patient has all of it.

2. Focused History — Beyond the Spine

- **Peripheral joints:** asymmetrical oligoarthritis, predominantly of the lower limbs.
- **Enthesitis** — inflammation where tendon meets bone. Ask about **heel pain**, at the Achilles insertion or the plantar fascia. It is the feature most often not connected to the back pain.
- **Dactylitis** — a uniformly swollen "sausage" digit, which is close to diagnostic of spondyloarthritis.
- **Acute anterior uveitis** — a unilateral, painful, red, photophobic eye with blurred vision. It recurs, and it occurs in up to a third of patients.

- **Psoriasis** — and **look for it yourself**, on the scalp, behind the ears, in the natal cleft, at the umbilicus, and in the nails for pitting and onycholysis. Patients frequently do not know they have it.
- **Inflammatory bowel disease** — diarrhoea, blood or mucus, weight loss.
- **Preceding gastrointestinal or genitourinary infection**, which raises reactive arthritis.
- Family history of spondyloarthritis, psoriasis, inflammatory bowel disease or uveitis. Smoking, which worsens outcome.

3. Physical Examination

- **Posture** — loss of lumbar lordosis, increased thoracic kyphosis, and in advanced disease the fixed "question mark" posture.
- **The measurements that matter, and how to do them:**
  - **Modified Schober test** — mark 10 cm above and 5 cm below the lumbosacral junction; on full forward flexion the distance should increase by more than 5 cm.
  - **Occiput-to-wall distance** — should be zero; any gap indicates fixed cervical flexion.
  - **Chest expansion** at the fourth intercostal space — **less than 5 cm is abnormal** and reflects costovertebral involvement.
  - Lateral lumbar flexion and cervical rotation.
- **Sacroiliac tenderness** and provocation with the flexion–abduction–external rotation manoeuvre.
- **Enthesitis sites**, dactylitis, peripheral joints, skin and nails, eyes.
- **Cardiac auscultation for aortic regurgitation**, and the chest for **apical pulmonary fibrosis** — both recognised extra-articular features.

4. Investigations

- **Radiographs of the sacroiliac joints** — sacroiliitis with erosion, sclerosis and eventual fusion. **They may remain normal for years after symptoms begin**, so a normal film excludes nothing in a young patient.
- **Magnetic resonance imaging of the sacroiliac joints with fat-suppressed sequences shows bone marrow oedema and detects active inflammation years before radiographic change.** This is what allows the diagnosis of **non-radiographic axial spondyloarthritis**, and it has transformed early diagnosis of this disease.
- **HLA-B27 supports the diagnosis but does not make it.** It is common in healthy people, with a prevalence that varies substantially between populations, so a positive result in an unselected patient with back pain means very little. Interpret it alongside the clinical picture.
- **C-reactive protein and erythrocyte sedimentation rate may be entirely normal despite active disease** — unlike rheumatoid arthritis. Normal inflammatory markers do not reassure here.

- Spinal radiographs in established disease: squaring of the vertebral bodies, shiny corners, syndesmophytes, and eventually the fused "bamboo spine".
- Baseline bloods and **tuberculosis and hepatitis screening before biologic therapy**.

5. Management

THE TREATMENT STUDENTS UNDER-RATE

Daily exercise and physiotherapy are the cornerstone of treatment in axial spondyloarthritis, not an adjunct to it.

Spinal extension exercises, postural work, hydrotherapy and maintained aerobic activity preserve mobility and function in a way no drug does. It is the most important intervention in this disease, it is free, and it is the one most often left out of the plan.

Prescribe it specifically — what exercises, how often, and with which physiotherapist — and review adherence as you would for a drug.

- **Non-steroidal anti-inflammatory drugs are the first-line drug therapy** and are strikingly effective; continuous use may slow radiographic progression. Prescribe with gastroprotection and attention to renal and cardiovascular risk.

WHAT DOES NOT WORK — AND IS PRESCRIBED ANYWAY

Methotrexate and sulfasalazine do not work for axial disease. They have a role only in peripheral arthritis.

Prescribing methotrexate for spinal symptoms is a common error carried over from rheumatoid arthritis, and it delays effective treatment while the patient continues to lose spinal mobility.

- **Biologic therapy for persistent active axial disease:** tumour necrosis factor inhibitors or interleukin-17 inhibitors. **Choose according to the extra-articular pattern** — monoclonal tumour necrosis factor inhibitors are preferred where there is uveitis or inflammatory bowel disease, and **interleukin-17 inhibitors are avoided in inflammatory bowel disease** because they may worsen it.
- **Uveitis: same-day ophthalmology assessment.** Give the patient a card and explicit instructions to attend an eye service directly, without a referral, whenever the eye becomes red and painful. Recurrent untreated uveitis causes permanent visual loss.
- Smoking cessation; **osteoporosis assessment**, since bone density is reduced despite the radiographic sclerosis; and surgery for hip disease or severe spinal deformity.

THE EMERGENCY TO REMEMBER

An ankylosed spine is a long rigid bone and it fractures with trivial trauma — typically at the cervicothoracic junction, and typically unstably, with a high risk of spinal cord injury.

Any patient with ankylosing spondylitis and new neck or back pain after even a minor fall requires urgent computed tomography or magnetic resonance imaging, not reassurance and analgesia. Plain films are unreliable in a fused spine.

Warn the patient, and remember it yourself when one arrives in the emergency department after falling from a chair.

6. Teaching Points and Viva Questions

- A young man whose back pain wakes him at four in the morning and improves with exercise does not have mechanical back pain.
- Ask about the heel, the toe and the eye — the diagnosis is often outside the spine.

- Look for psoriasis yourself, in the places patients do not look.
- Normal radiographs and normal inflammatory markers exclude nothing; magnetic resonance imaging makes the early diagnosis.
- HLA-B27 supports, it does not diagnose.
- Exercise is the treatment. Methotrexate is not.
- A fused spine after a minor fall needs cross-sectional imaging.

Questions you should be able to answer:

- List the features of inflammatory back pain and apply them to this patient.
- Describe how you perform the modified Schober test and what a normal result is.
- His radiographs are normal but the history is classical. What do you do next?
- He also has ulcerative colitis. How does that influence your choice of biologic?
- He falls from a standing height and complains of neck pain. What is your concern and your action?

Case 61 · Vasculitis

CLINICAL VIGNETTE

A **62-year-old man** has had three months of malaise, intermittent fever, aching joints and 9 kg of weight loss. For six weeks he has had a **blocked, crusting nose with blood-stained discharge**, treated twice as sinusitis. For two weeks he has coughed up small amounts of blood. Last week his **right foot became painful and numb and he began tripping over it**.

On examination: temperature 37.9 °C. **Nasal crusting with septal ulceration.** The left eye is red and painful. There is a **palpable purpuric rash over both shins** and a **right common peroneal nerve palsy with foot drop**. Blood pressure 148/92 mmHg.

Urine dipstick: blood +++, protein ++; microscopy shows red cell casts. Creatinine 240 µmol/L (normal six months ago) · C-reactive protein 160 · **proteinase-3 ANCA strongly positive**. Chest radiograph: bilateral nodules, one cavitating.

THE PATTERN THAT MAKES THE DIAGNOSIS

A multisystem illness with constitutional symptoms, a high C-reactive protein, an abnormal urine dipstick and no infection found is a vasculitis until proved otherwise.

Look for the combination: **upper airway disease · lung disease · glomerulonephritis · palpable purpura · mononeuritis multiplex · inflammatory eye disease.** No single feature is diagnostic; the pattern is.

Two findings deserve special weight. Mononeuritis multiplex — asymmetrical, painful, stepwise involvement of named nerves — is close to specific for vasculitis (or diabetes). And **"resistant sinusitis" with systemic features is granulomatosis with polyangiitis** far more often than it is stubborn sinusitis: **examine the nose in every suspected vasculitis.**

1. Think First — Classify by Vessel Size

Size	Diseases and their signature
Large vessel	Giant cell arteritis — over 50, temporal headache, scalp tenderness, jaw claudication, visual loss, high inflammatory markers. Takayasu arteritis — younger, absent pulses, limb claudication, bruits, blood pressure differences between arms.
Medium vessel	Polyarteritis nodosa — skin, nerve, gut and renal artery involvement, hypertension, associated with hepatitis B; typically spares the lungs and is ANCA-negative. Kawasaki disease in children.
Small vessel, ANCA-associated	Granulomatosis with polyangiitis — upper airway, lung, kidney; usually PR3-ANCA. Microscopic polyangiitis — kidney and lung without granulomatous upper airway disease; usually MPO-ANCA. Eosinophilic granulomatosis with polyangiitis — late-onset asthma, nasal polyps, marked eosinophilia, neuropathy and cardiac involvement.
Small vessel, immune complex	IgA vasculitis — purpura on buttocks and legs, arthralgia, abdominal pain, nephritis. Cryoglobulinaemic vasculitis — associated with hepatitis C, low complement. Anti-glomerular basement membrane disease — pulmonary haemorrhage with nephritis.
Variable vessel	Behçet disease — recurrent painful oral and genital ulceration, uveitis, pathergy, and a distinctive tendency to venous thrombosis including at unusual sites. Not rare in this region and easily overlooked.
Secondary and mimics	Connective tissue disease; infection — infective endocarditis, hepatitis B and C, HIV, tuberculosis; drugs — hydralazine, propylthiouracil, and cocaine adulterated with levamisole; malignancy.

2. Focused History

- Constitutional: fever, weight loss, night sweats, malaise, arthralgia and myalgia.
- **Upper airway:** nasal crusting and obstruction, epistaxis, hearing loss, hoarseness, and **stridor from subglottic stenosis**.

- **Chest:** haemoptysis, breathlessness, late-onset asthma.
- **Kidney:** frothy or bloody urine, oedema, hypertension — usually silent, hence the dipstick.
- **Skin:** palpable purpura, ulcers, digital ischaemia, livedo, nodules.
- **Nerve:** numbness or weakness in the territory of named nerves, in a stepwise asymmetrical pattern.
- **Eye:** red painful eye, scleritis, visual loss. **Gut:** abdominal pain, which may mean mesenteric ischaemia.
- **Large vessel questions specifically:** temporal headache, scalp tenderness, **jaw claudication**, visual symptoms, limb claudication.
- **Drugs, hepatitis and HIV risk, and intranasal cocaine** — each produces a convincing vasculitis mimic.

3. Physical Examination

- **Blood pressure in both arms, all peripheral pulses, and auscultation for bruits**; temporal artery tenderness, thickening and pulsation.
- **The nose and upper airway** — crusting, septal ulceration or perforation, saddle deformity.
- Eyes; skin including the shins and digits; **a full neurological examination mapping any deficit to named nerves**; chest; and **a urine dipstick performed by you**.

4. Investigations

- **Immediately:** urinalysis with microscopy, creatinine **with its trend**, C-reactive protein and erythrocyte sedimentation rate, complete blood count (**eosinophilia** in eosinophilic granulomatosis with polyangiitis), chest radiograph.
- **Immunology, sent urgently: ANCA — both proteinase-3 and myeloperoxidase** — anti-glomerular basement membrane antibody, antinuclear and anti-double-stranded DNA antibodies, complement, cryoglobulins, immunoglobulins, rheumatoid factor.
- **Infection screen, which is not optional: blood cultures, echocardiography, hepatitis B and C, HIV, and tuberculosis assessment.**
- **Tissue wherever it can be obtained:** renal biopsy, nasal or lung biopsy, skin biopsy, nerve or muscle biopsy; **temporal artery biopsy or ultrasound** in suspected giant cell arteritis.
- **Imaging:** computed tomography of the chest (nodules, cavitation, alveolar haemorrhage) and sinuses; and in large vessel disease, vascular ultrasound, magnetic resonance angiography or positron emission tomography.
- **ANCA supports the diagnosis but does not make it, a negative ANCA does not exclude it, and the titre is an unreliable guide to relapse.** Tissue and the clinical picture remain the arbiters.

THE MIMIC THAT MUST BE EXCLUDED FIRST

Infective endocarditis reproduces vasculitis almost exactly — fever, weight loss, raised inflammatory markers, purpura, splinter haemorrhages, glomerulonephritis, positive rheumatoid factor, low complement, and even a positive ANCA.

Immunosuppressing a patient with endocarditis is catastrophic. So take blood cultures and arrange echocardiography **before** high-dose steroids, in every patient in whom the diagnosis is not already secure. Tuberculosis and HIV deserve the same caution.

This is the single commonest way that a confident vasculitis diagnosis goes badly wrong.

TWO SITUATIONS THAT WILL NOT WAIT

Pulmonary–renal syndrome — haemoptysis with an active urinary sediment — or a **creatinine rising over days**, is an emergency. **Same-day nephrology and rheumatology involvement, urgent ANCA and anti-glomerular basement membrane antibody, urgent biopsy — and where suspicion is high, immunosuppression started before the results**, with plasma exchange for anti-glomerular basement membrane disease and severe alveolar haemorrhage. See Case 33.

Giant cell arteritis with any visual symptom — high-dose corticosteroid immediately and same-day ophthalmology. Do not wait for the biopsy: it remains informative for a week or two after steroids are started, whereas the vision does not come back. See Seminar 5.

5. Management

- **Induction for organ-threatening ANCA-associated vasculitis:** high-dose corticosteroid with **rituximab or cyclophosphamide**; plasma exchange in selected severe renal disease and pulmonary haemorrhage; **avacopan** as a complement-pathway inhibitor allowing substantial steroid sparing.
- **Maintenance for years**, with rituximab, azathioprine, methotrexate or mycophenolate. **Relapse is common**, which is why follow-up is lifelong.

TREATING THE TREATMENT

The treatment causes as much harm as the disease if it is not managed deliberately.

Co-trimoxazole for Pneumocystis prophylaxis · bone protection · gastric protection · glucose monitoring · vaccination **before** immunosuppression where possible · **screening for hepatitis B and latent tuberculosis before rituximab**.

Cyclophosphamide specifically: infertility — offer gamete storage before the first dose — haemorrhagic cystitis, later bladder cancer, and marrow suppression. The fertility conversation must happen at the start, not after four cycles.

- **Giant cell arteritis:** corticosteroid with **tocilizumab** as a steroid-sparing agent, tapering over 12 to 18 months, with bone protection throughout.
- **Takayasu arteritis:** corticosteroid with a steroid-sparing agent, vascular imaging surveillance, and **blood pressure measured in the limb with the best flow**, since a subclavian stenosis will give a falsely low reading.
- **Behçet disease:** colchicine for mucocutaneous disease; immunosuppression or anti-tumour-necrosis-factor therapy for ocular, neurological or vascular involvement; urgent ophthalmology for uveitis.
- **Monitoring: symptoms, C-reactive protein, creatinine and a urine dipstick at every single visit.** The dipstick is the cheapest and earliest detector of renal relapse.

6. Teaching Points and Viva Questions

- Multisystem illness plus a high C-reactive protein plus an abnormal urine is vasculitis until proved otherwise.

- Examine the nose and dipstick the urine — both take seconds and both change the diagnosis.
- Mononeuritis multiplex is nearly specific for vasculitis or diabetes.
- Take blood cultures and an echocardiogram before high-dose steroids.
- ANCA supports, does not prove, and does not reliably track relapse.
- Start steroids in giant cell arteritis before the biopsy.
- Offer gamete storage before cyclophosphamide.

Questions you should be able to answer:

- Which six features of this presentation together make a vasculitis likely?
- What does his foot drop represent, and why is it useful diagnostically?
- What must be excluded before you give him methylprednisolone, and how?
- His ANCA is negative but the picture is unchanged. Does that alter your management?
- He is 62 and wants to know about fertility before cyclophosphamide. What do you offer?

Case 62 · Gout and Calcium Pyrophosphate Deposition Disease

CLINICAL VIGNETTE

A **56-year-old man** presents with his fourth attack in two years. Three days ago he woke at 4 a.m. with pain in the right great toe, which within a few hours became so severe that he could not bear the weight of a bedsheet. Previous attacks affected the same joint and, once, the left knee.

He takes bendroflumethiazide for hypertension, drinks five or six beers most evenings, and has chronic kidney disease with an estimated filtration rate of 48.

On examination: body mass index 33 kg/m^2, blood pressure 152/94 mmHg. The right first metatarsophalangeal joint is red, hot, swollen and exquisitely tender. **There are firm chalky nodules on the helix of the right ear and over both olecranon processes.**

Serum urate 520 µmol/L. Joint aspirate: negatively birefringent needle-shaped crystals; Gram stain and culture negative.

1. Recognising It

- **The attack:** abrupt onset, often waking the patient in the early hours, **maximal within 12 to 24 hours**, with pain out of all proportion to the size of the joint, and self-limiting over seven to ten days even untreated.
- **The joints:** the first metatarsophalangeal joint — podagra — then the instep, ankle and knee. Chronic disease becomes polyarticular and involves the upper limbs, and can closely mimic rheumatoid arthritis.
- **Tophi** — firm chalky deposits on the **helix of the ear, the olecranon, the Achilles tendon, the finger pulps and extensor surfaces**. Look for them; they establish that this is longstanding disease requiring urate-lowering therapy.
- **Provoking factors:** alcohol, especially beer and spirits; purine-rich food; dehydration; **diuretics**; surgery and acute illness; and, paradoxically, **the initiation of urate-lowering therapy**.
- **Drugs that raise urate:** thiazide and loop diuretics, low-dose aspirin, ciclosporin and tacrolimus, pyrazinamide and ethambutol.
- **Comorbidity, which is the reason gout matters beyond the joint:** chronic kidney disease, hypertension, obesity, the metabolic syndrome, ischaemic heart disease and heart failure. **Gout is a marker of cardiovascular risk and should trigger its assessment.**

2. Investigations

- **Joint aspiration with polarised microscopy is definitive** — negatively birefringent needle-shaped crystals — **and it simultaneously excludes septic arthritis, which coexists with gout** (Seminar 6).

THE SERUM URATE, AND WHY THE TIMING MATTERS

A normal urate during an acute attack does not exclude gout, because levels commonly fall during the attack. **And a raised urate does not diagnose it**, because most hyperuricaemic people never develop gout.

So measure the urate four to six weeks after the attack has settled, to establish a baseline and a treatment target — not during it, when the number will mislead in either direction.

- Renal function, glucose, lipids, complete blood count and liver function — for the comorbidity and to guide drug choice.
- **Radiographs in chronic disease:** periarticular erosions with **overhanging edges and preserved joint space**. Ultrasound (the double contour sign) and dual-energy computed tomography where the diagnosis is uncertain and aspiration is not possible.

3. Treating the Attack

- **Any one of an anti-inflammatory drug, colchicine, or a corticosteroid — and the choice is made by comorbidity, not by preference.**
- **In this patient, with chronic kidney disease and hypertension, an anti-inflammatory drug is a poor choice.** Colchicine requires **dose reduction in renal impairment** and interacts dangerously with statins, macrolides, ciclosporin and verapamil. **Oral or intra-articular corticosteroid is often the safest option**, and an intra-articular injection is ideal for a single accessible joint once sepsis is excluded.
- Treat within hours rather than days; rest, ice and elevation help.

THE INSTRUCTION MOST OFTEN GOT WRONG ON THE WARD

Do not start urate-lowering therapy during an acute attack — but if the patient is already taking allopurinol, do not stop it either.

Stopping allopurinol during a flare prolongs the attack and destabilises long-term control, and it is one of the commonest errors made on admission. The drug continues; the flare is treated alongside it.

4. Urate-Lowering Therapy — the Part Done Badly

- **Indications:** two or more attacks a year, **tophi**, chronic gouty arthropathy, radiographic joint damage, urate renal stones, chronic kidney disease, or diuretic therapy that cannot be withdrawn. **This patient qualifies several times over.**

TREAT TO A TARGET, NOT TO A DOSE

Start allopurinol low — 100 mg, or 50 mg in chronic kidney disease — and titrate upwards every two to four weeks against the measured urate.

Treat to target: a serum urate below 360 µmol/L, or below 300 µmol/L where there are tophi or severe disease. Crystals dissolve below the saturation point and tophi shrink; above it, they do not.

"Allopurinol did not work" almost always means allopurinol was left at 100 or 300 mg without anyone measuring the urate. The dose is whatever achieves the target, and in many patients that is 400 to 600 mg or more.

- **Cover the first three to six months of urate-lowering therapy with colchicine or an anti-inflammatory drug**, because mobilising urate provokes flares — **and warn the patient that attacks may initially increase.** Without that warning they will conclude the drug is causing the problem and stop it.
- **Never stop urate-lowering therapy because of a flare.** Explain at the outset that treatment is long term and that gout becomes, in practice, a curable disease once urate is held below target.
- **Febuxostat** where allopurinol is not tolerated, with caution in established cardiovascular disease; uricosuric agents; and pegloticase in refractory tophaceous disease. **Consider HLA-B*5801 testing before allopurinol in populations where it is prevalent**, because of the risk of severe cutaneous reactions.

- **Review the diuretic** — switching to an alternative antihypertensive is often the single most useful change, and **losartan and calcium channel blockers lower urate** while thiazides raise it.
- Weight reduction, reduction of beer, spirits and sugar-sweetened drinks, hydration, and treatment of the cardiovascular and metabolic risk.

CALCIUM PYROPHOSPHATE DEPOSITION DISEASE — "PSEUDOGOUT"

Older patients, and different joints — typically the knee and wrist rather than the great toe.

Aspirate shows positively birefringent rhomboid crystals, and radiographs show **chondrocalcinosis**.

Acute attacks are treated exactly as for gout, but **there is no role for urate-lowering therapy**.

In a young patient, or where the disease is florid, look for an underlying cause: haemochromatosis, hyperparathyroidism, hypomagnesaemia or hypophosphatasia.

5. Teaching Points and Viva Questions

- Aspirate to confirm the crystals and to exclude sepsis — they coexist.
- A normal urate during an attack means nothing; measure it six weeks later.
- Choose the acute drug by the comorbidity, not by habit.
- Never stop allopurinol during a flare.
- Titrate allopurinol to a urate target, and cover the first months with prophylaxis.
- Warn the patient that attacks may increase at first, or they will stop the drug.
- Look for tophi, and review the diuretic.

Questions you should be able to answer:

- Why would you avoid an anti-inflammatory drug in this man, and what would you give instead?
- He is admitted with an attack while taking allopurinol. What do you do with it?
- What is your urate target here, and how will you get there?
- He returns after six weeks of allopurinol saying it has made his gout worse. What has happened and what do you say?
- A 78-year-old has an acute hot knee with rhomboid crystals. What is the diagnosis and does he need allopurinol?

Case 63 · Antiphospholipid Syndrome

CLINICAL VIGNETTE

A **32-year-old woman** is referred after a **second unprovoked deep vein thrombosis**. The first was at the age of 26, while she was taking the combined oral contraceptive pill.

Her obstetric history is of **three first-trimester miscarriages** and a **stillbirth at 24 weeks** with placental insufficiency. She has migraine with aura.

On examination: a mottled, net-like purplish discolouration over both thighs — **livedo reticularis**. No synovitis, no rash elsewhere. Blood pressure 138/86 mmHg.

Platelets 96 × 10^9/L · activated partial thromboplastin time prolonged and does not correct on mixing with normal plasma · lupus anticoagulant positive · anticardiolipin IgG high · anti-beta-2 glycoprotein I high — all confirmed on a repeat sample 12 weeks later. Antinuclear antibody weakly positive, anti-double-stranded DNA negative.

THE DEFINITION, AND WHY THE REPEAT TEST MATTERS

Thrombosis, or defined pregnancy morbidity, plus persistently positive antiphospholipid antibodies on two occasions at least 12 weeks apart.

The 12-week interval is not a formality. Antiphospholipid antibodies appear transiently after infection and in many healthy people, and a single positive result labels a patient with a lifelong diagnosis and lifelong anticoagulation on inadequate evidence. **Never diagnose the syndrome on one sample.**

The three antibodies: lupus anticoagulant, anticardiolipin, and anti-beta-2 glycoprotein I. **"Triple positive" carries the highest risk of recurrence** and the strongest indication for warfarin over other agents.

1. The Clinical Features

Domain	Features
Venous thrombosis	Deep vein thrombosis and pulmonary embolism — and thrombosis at unusual sites: cerebral venous sinus, splanchnic, hepatic, retinal. Unusual-site thrombosis in a young person should always prompt testing.
Arterial thrombosis	Stroke or transient ischaemic attack in a young person without conventional risk factors; myocardial infarction; limb ischaemia.
Obstetric	Three or more consecutive miscarriages before 10 weeks · one or more fetal deaths after 10 weeks · delivery before 34 weeks for pre-eclampsia or placental insufficiency.
Haematological	Thrombocytopenia — and note the paradox that these patients clot despite a low platelet count — and autoimmune haemolytic anaemia.
Skin	Livedo reticularis, skin ulcers, digital ischaemia and gangrene.
Cardiac	Valve thickening and non-infective (Libman–Sacks) vegetations, which may embolise.
Neurological	Migraine, chorea, cognitive impairment, transverse myelitis, seizures.
Renal	Antiphospholipid nephropathy with hypertension and proteinuria.

- **Primary**, or **secondary to systemic lupus erythematosus** and other autoimmune disease — so screen for lupus in every patient (Case 59).

THE LABORATORY PARADOX

A prolonged activated partial thromboplastin time that does not correct on mixing, in a patient who thromboses rather than bleeds.

The lupus anticoagulant is an in-vitro artefact — it interferes with phospholipid-dependent clotting assays — while in vivo it is **prothrombotic**. Students reasonably expect a prolonged clotting time to mean bleeding, and here it means the opposite.

Two practical consequences: anticoagulation and an acute thrombosis both interfere with the assays, so **timing of the test matters**; and the prolonged time should not prompt transfusion of plasma.

2. Catastrophic Antiphospholipid Syndrome

EMERGENCY

Thrombosis in three or more organs within days to a week, with microvascular occlusion and multiorgan failure. Rare, and with a high mortality.

The usual triggers are infection, surgery, pregnancy, and — importantly — withdrawal or interruption of anticoagulation.

Treatment: full anticoagulation, high-dose corticosteroid, and plasma exchange or intravenous immunoglobulin, with treatment of the trigger and critical care support.

Which is the practical reason never to stop anticoagulation abruptly in these patients, and to plan perioperative bridging carefully rather than simply omitting doses.

3. Management

THE ANTICOAGULANT CHOICE

Anticoagulate with a vitamin K antagonist. Direct oral anticoagulants are inferior in antiphospholipid syndrome — particularly in triple-positive patients and in arterial thrombosis — and should be avoided.

This is one of the few remaining firm indications for warfarin in venous thromboembolism, and it is easily missed when a young woman with a deep vein thrombosis is started on a direct oral anticoagulant before anyone has asked why she clotted. **The obstetric history is the clue that should prompt testing** (Seminar 11).

- **Duration: indefinite** after an unprovoked thrombosis in confirmed antiphospholipid syndrome. In arterial events, anticoagulation is used, sometimes with aspirin, and a higher target range is considered after recurrence.
- **Antibody-positive but never thrombosed: do not anticoagulate.** Consider low-dose aspirin in high-risk profiles, and concentrate on modifiable risk — **stop smoking, avoid oestrogen-containing contraception, treat hypertension and lipids, and give thromboprophylaxis around surgery, immobility and pregnancy.**

PREGNANCY

Aspirin plus low-molecular-weight heparin from early pregnancy, continued for six weeks after delivery.

Warfarin is teratogenic and direct oral anticoagulants are contraindicated in pregnancy — so the anticoagulant must be changed **before** conception, not after a positive test.

Joint obstetric and rheumatology care throughout; hydroxychloroquine may improve outcomes; and close surveillance for **pre-eclampsia and fetal growth restriction**.

Plan the pregnancy rather than react to it. For a 32-year-old with three miscarriages and a stillbirth, this conversation is the most valuable thing in the consultation.

- Screen for systemic lupus erythematosus; consider hydroxychloroquine; correct vitamin D; and manage cardiovascular risk actively, since these patients have accelerated arterial disease.

4. Teaching Points and Viva Questions

- Unprovoked thrombosis in a young person, thrombosis at an unusual site, or recurrent pregnancy loss should prompt testing.
- Confirm on a second sample at least 12 weeks later. Never diagnose on one.
- A prolonged activated partial thromboplastin time that does not correct, in a patient who clots.
- Warfarin, not a direct oral anticoagulant.
- Heparin and aspirin in pregnancy, changed over before conception.
- Do not anticoagulate asymptomatic antibody positivity.
- Interrupting anticoagulation can precipitate catastrophic disease.

Questions you should be able to answer:

- Which parts of her history should have prompted testing after the first thrombosis?
- Why was the test repeated at 12 weeks?
- Explain how a patient with a prolonged clotting time thromboses.
- She was started on rivaroxaban in the emergency department. What do you do and why?
- She wants to conceive next year. Set out your plan over the next twelve months.