

050

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Notes & Notes for MRCP

By Dr. Yousif Abdallah Hamad

□ serious allergic reactions (including a rash over the whole body, shortness of breath, wheezing, dizziness, swelling around the mouth or eyes, fast pulse, and sweating), □ alveolar hemorrhage, acute respiratory distress syndrome, and hemoptysis. □ Severe sickle cell crises, in patients with sickle cell disorders. Sargramostim • Action □ granulocyte macrophage colony-stimulating factor (GM-CSF) • It is produced in yeast • stimulate other myeloid and megakaryocyte • Indications □ for myeloid reconstitution after bone marrow transplantation. □ neutropenia induced by chemotherapy • side effects □ GM-CSF can cause more severe effects, including fever, arthralgias, and capillary damage with edema. □ edema

Updated 2022

Third edition Notes & Notes

For MRCP By Dr. Yousif Abdallah Hamad Volume 3

Foreword

With the grace of the Almighty Allah, I have introduced the third edition of the popular book, the Notes & Notes for MRCP Part & 2. The MRCP exam requires a wide range of information, particular thinking, and question directed experience. This book is directed mainly at those who need comprehensive revision of the topics which commonly appear in the written MRCP exams. It will be helpful to go through these topics before you start solving the best of the five questions; it is also recommended to go quickly over this book in the last few weeks before the day of your exam. This new edition contains the new published guidelines.

I hope you will find the maximum benefits from this book to get through MRCP written exams.

To practice the best of five questions we advise you to join the best website for MRCP passonexam.com For any enquiry or comment, please do not hesitate to contact me.

“The mind is not a vessel to be filled, but a fire to be kindled.” — Plutarch.

March - 2022 Dr. Yousif Abdallah Hamad
Internal medicine specialist – Sudan medical counsel
MRCPS- Glasgow- UK MRCP- Ireland
Dryousif23 @gmail.com <https://www.facebook.com/dryousif23>

The 10 Golden Tips for MRCP written exams you will ever need

1. For MRCP, do not read hard; read smart.
2. Three to six months is usually enough for preparation.
3. Practice the best of the five questions as much as possible.
4. The few days before the exam date, stop revising questions and concentrate on your MRCP notes and top tips.
5. Remember, you are getting ideas and concepts from the questions.
6. Time factor in the exam room is the leading killer after poor preparation.
7. Manage your time wisely.
8. Read the end of the question first; if you can answer it without reading the whole scenario, it will save your time for the other tuff question (long scenario, .what is the action of imatinib?)
9. Take care for any single word in the question, e.g. (the initial test, the diagnostic test, the best test, the next step)
10. Practice, practice and practice.

Contents Chapter 8 Rheumatology Rheumatoid factor	Rheumatoid arthritis
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Compartment syndrome	Complex regional pain syndrome (CRPS) Dactylitis / De Quervain's tenosynovitis Gout
..... Hip pain in adults	Hip problems in children
Lateral epicondylitis / Lower back pain Mixed connective tissue disease (MCTD) Osteoarthritis	Osteomyelitis
..... Discitis / Osteomalacia	Osteopetrosis / Osteoporosis
Paget's disease of the bone	Penicillamine
Pseudogout / Psoriatic arthropathy	Reactive arthritis (Reiter syndrome)
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..... Sjogren's syndrome	Chapter 9 Infectious diseases Classification of bacteria
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Streptococci Bacteria and growing media / Enterococcus
Vancomycin-resistant enterococci / Anthrax	Diphtheria
Listeria Campylobacte / Shigella
Escherichia coli	Incubation periods / Virulence factors

Systemic lupus erythematosus (SLE) Drug-induced lupus erythematosus
 Antiphospholipid syndrome Antiphospholipid syndrome: pregnancy Juvenile
 idiopathic arthritis (JIA).....

Adult onset Still's disease (AOSD) (Adult Still's disease) Raynaud's
 Systemic sclerosis (SSc) Morphea
 (localised scleroderma) Polymyalgia rheumatica (PMR) Temporal
 arteritis (Giant cell arteritis (GCA) Polyarthritis / Polyarteritis nodosa (PAN) Granulomatosis with
 polyangiitis (Wegener's granulomatosis) Microscopic Polyangiitis / Churg-Strauss syndrome
 Idiopathic pulmonary haemosiderosis Henoch-Schonlein purpura
 Kawasaki disease Takayasu's arteritis
 Buerger's disease IBD-associated arthropathy
 SAPHO syndrome Elbow pain
 Shoulder problems / Polymyositis Dermatomyositis Inclusion
 body myositis (IBM) Fibromyalgia (FM) Dupuytren's
 contracture Baker cyst Plasmids
 Antibiotic resistance mechanism / Tetanus Salmonella
 & Typhoid fever Meningitis
 Encephalitis Meningococcal septicaemia / Sepsis
 Tuberculosis (TB) TB Drug therapy
 Latent tuberculosis infection (LTBI) Miliary TB
 Non-tuberculous mycobacterial infections

Multidrug-resistant tuberculosis (MDR-TB)..... Leprosy / Vaccinations Post-
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 disease (CSD) / Whooping cough (pertussis) Acute epiglottitis..... Cellulitis
 Methicillin-resistant Staphylococcus aureus (MRSA) Necrotising
 fasciitis Toxic shock syndrome (TSS) Cholera
 Congenital infections Chickenpox
 (Varicella-zoster virus) Cytomegalovirus Dengue fever
 Herpes simplex virus Yellow fever
 Human immunodeficiency virus (HIV) HIV and pregnancy
 HIV: anti-retrovirals HIV lipodystrophy
 (Antiretroviral-related lipodystrophy) HIV: diarrhoea HIV
 nephropathy Cryptococcal disease in AIDS (Cryptococcosis) HIV: immunisation
 HIV: Kaposi's sarcoma HIV: Dermatologic
 conditions (Eosinophilic folliculitis) (EF) HIV: abnormal vaginal bleeding CMV retinitis in
 a patient with HIV / Vaginal discharge Bacterial vaginosis (BV) Trichomonas
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 Acanthosis nigricans Acne rosacea / Acne vulgaris
 Isotretinoin Alopecia / Alopecia areata
 Pemphigus vulgaris Bullous pemphigoid
 Dermatitis herpetiformis (DH) Discoid lupus erythematosus
 Contact dermatitis Pruritus / Eczema herpeticum
 Eczema: topical steroids Pompholyx / Erythema ab igne

Genital ulcers (STI) Genital herpes / Chancroid
Lymphogranuloma venereum (LGV) Syphilis Genital
warts / Chlamydia genitourinary infections Gonorrhoea
Toxoplasmosis H1N1 influenza pandemic
Infectious mononucleosis & (Epstein-Barr virus) Parvovirus B19
Leishmaniasis Leptospirosis Lyme
disease Lymphadenopathy / Malaria Measles
..... Rubella / Parotitis / Parotid swelling Orf / Pelvic
inflammatory disease(PID) Psittacosis (ornithosis) / Pyogenic liver abscess Pyrexia of
unknown origin / Q fever Rabies Scabies
..... Helminths
Schistosomiasis Strongyloides stercoralis / Tape worms
Trypanosomiasis Nematodes
Filariasis Loiasis Animal
bites / Rocky Mountain spotted feve Histoplasmosis Actinomycosis /
Malignant otitis externa

Erythema multiforme

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) Erythema nodosum
..... Erythema induratum (EI) / Erythrasma / Erythroderma Fungal nail
infections Beau's lines / Granuloma annulare
Herpes simplex virus / Molluscum contagiosum Impetigo
Erysipelas Koebner phenomenon / Lichen planus Lichen
sclerosus Lichen simplex chronicus (LSC) / Lichen amyloidosis
Onycholysis / Parvovirus B19/ Pityriasis rosea

Pityriasis versicolor / Psoriasis Psoriasis: guttate
Pyoderma gangrenosum Scabies
Seborrhoeic dermatitis Skin disorder in pregnancy Skin
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..... Angular stomatitis / Venous ulceration Pressure
ulcers Keloid scars

Chapter 11 Psychiatry Eating disorders: Anorexia nervosa Eating disorders: Bulimia
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(NMS) Serotonin syndrome Antidepressants
..... Selective serotonin-norepinephrine reuptake inhibitors Serotonin
antagonist and reuptake inhibitors (SARIs) Monoamine oxidase inhibitors (MAOIs) Tricyclic
antidepressants (TCA) Atypical antidepressants
Benzodiazepines Post-traumatic stress disorder Post-
concussion syndrome / Grief reaction Depression: screening and assessment Suicide /
Depression in older people Chapter 12 Ophthalmology Acute angle closure glaucoma
(AACG) Primary open-angle glaucoma (POAG) Age related macular degeneration
(AMD) Cataracts Angioid retinal streaks
..... Mydriasis Holmes-Adie pupil / Argyll-

Robertson pupil Anisocoria / Optic atrophy Optic neuritis
..... Relative afferent pupillary defect Herpes simplex
keratitis / Herpes zoster ophthalmicus Blepharitis / Keratitis Red eye
..... Scleritis / Episcleritis

Increased skin fragility / Basal cell carcinoma (BCC) Squamous cell carcinoma (SCC)
Keratoacanthoma (KA) Actinic keratoses / Malignant melanoma Moles /
Systemic mastocytosis / Angiosarcoma Pyogenic granuloma Skin
disorders associated with malignancy Otitis externa / Livedo reticularis (LR) Hyperhidrosis /
Seborrheic keratosis Solar keratosis / Telogen phase

Generalised anxiety disorder Mood disorder
Cognitive behavioural therapy Seasonal affective disorder (SAD) Body
dysmorphic disorder Post-partum mental health problems Alcohol -
problem drinking: management Alcohol withdrawal Schizophrenia
..... Electroconvulsive therapy (ECT) Charles Bonnet
syndrome (CBS) Delusions / Personality disorders Panic disorder
..... Acute confusional state Hypnagogic and
hypnopompic hallucinations

Conjunctivitis / Subconjunctival haemorrhage Posterior uveitis / Retinitis Retinitis
pigmentosa Sudden painless loss of vision Tunnel vision /
Ectopia lentis Fundoscopic features in eye infections Eye signs in Systemic
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Chapter 13 Pharmacology Pharmacokinetics: metabolism / Drug absorption First-pass metabolism /
Drug kinetics Zero-order kinetics Acetylator status / Half-life
..... Trough level / Affinity & efficacy Dosage intervals
..... Clinical trial: phases Prodrugs
..... P450 enzyme system Drugs required
therapeutic monitoring Drug causes gingival hyperplasia Drugs causing
photosensitivity Drugs causing specific skin reactions Drug affects folic acid
metabolism Drug causes SIADH / Drug causes of urticaria Drugs induced
galactorrhoea Drugs associated with gynaecomastia Drug-induced
impaired glucose tolerance Drug-induced lupus erythematosus Drug-induced
Pancytopenia Drug-induced thrombocytopenia / Sulfa drugs Disulfiram
..... Drug-induced long QT / Drugs causing ocular problems Drug
induced photosensitivity / Drug induced ototoxicity Drug induced seizures
Drug causes erythema multiforme, and the Stevens-Johnson syndrome subtype. Drugs
which act on serotonin receptors Drugs that can be cleared with Hemodialysis Prescribing in
patients with heart failure Antiarrhythmics: Vaughan Williams classification Atropine / Adenosine
..... Flecainide Amiodarone
..... Dobutamine & Dopamine / Adrenaline Antiplatelets
..... Acetylsalicylic acid (ASA, aspirin) Salicylate overdose
..... Clopidogrel IIb/IIIa inhibitors (eg:
Abciximab) Phosphodiesterase III (PDE) inhibitors (dipyridamole & cilostazol)

Angiotensin-converting enzyme (ACE) inhibitors Adrenoceptor antagonists / Beta-blockers
 Calcium channel blockers Centrally acting antihypertensives / Bosentan

 Nitroglycerin / Nicorandil Digoxin and digoxin toxicity
 Diuretics Bendroflumethiazide
 Amiloride / Triamterene / Spironolactone Eplerenone / Diuretic abuse / Theophylline Antimuscarinic
 agent Tiotropium / Doxapram / Sodium cromoglicate Magnesium
 treatment in asthma Anti-convulsants Sodium valproate
 / Phenytoin Carbamazepine Vigabatrin / Topiramate /
 Gabapentin Levetiracetam (Keppra) / Prochlorperazine / Barbiturates Anticholinergic syndrome
 Serotonin syndrome / Oculogyric crisis St John's Wort / Dopamine
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 Selective serotonin reuptake inhibitors (SSRIs) Lithium
 Lithium toxicity Therapeutic drug monitoring / Baclofen
 Octreotide / Orlistat Prescribing in pregnant patients
 Combined oral contraceptive pills Breast feeding: contraindications Drug
 causes teratogenesis Antibiotics: bactericidal vs. bacteriostatic Antibiotics:
 mechanisms of action Skin rash with antibiotics / Co-trimoxazole Aminoglycosides
 Macrolides Erythromycin /
 Quinolones Co-amoxiclav / Probenecid / Sulfonamides Vancomycin
 Linezolid Carbapenems /
 Trimethoprim Quinupristin & dalfopristin antibiotics Tuberculosis: drug
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 Griseofulvin / Diethylcarbamazine Overdose of antimalarial medications Chloroquine
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 Measurement of drug concentrations Drug toxicity in renal failure
 Characteristic smells of toxins/poisons Arsenic toxicity
 Drugs altered pupil size / Charcoal Methanol poisoning
 Ethylene glycol toxicity Isopropyl alcohol (Isopropanol) intoxication Ecstasy
 poisoning / Opioid misuse Morphine / Pethidine Buprenorphine
 / Cocaine Heroin withdrawal Benzodiazepine
 overdose / Cathinone toxicity Cannabinoids / Cyanide poisoning Sarin gas
 Arsenic / Acid poisoning / Alkali poisoning Radiosensitiser
 drugs Management of body packers Chapter 14
 Biochemistry & metabolism

 Anion gap (AG) Metabolic alkalosis
 Respiratory acidosis Respiratory alkalosis
 Hyperkalaemia Pseudohyperkalaemia

Hypokalaemia and acid-base balance Hypernatraemia / Hyponatraemia.....
Hypomagnesaemia Hypermagnesaemia
Hypophosphataemia Hyperphosphataemia
Collagen Types / Vitamin B3 (Niacin) deficiency

Heavy metal poisoning / Lead poisoning Mercury poisoning / Cadmium (Cd) poisoning Thallium
poisoning / Iron overdose LSD intoxication / New recreational drugs Paracetamol overdose
..... Paraquat poisoning Organophosphate insecticide
poisoning Carbon Monoxide (CO) Poisoning Antiemetics
..... 5-HT₃ antagonists Antihistamines
..... Human and animal bite / Botox D-Penicillamine /
Isotretinoin Cinnarizine / Ergotamine Finasteride /
Acetazolamide Bicarbonate therapy / Bisphosphonates Botulinum toxin /
Immunoglobulins: Therapeutics Malignant hyperthermia (MH) Intravenous fluid
therapy Lactulose Bismuth / Non-
steroidal anti-inflammatory drugs (NSAID) Celecoxib
Aminosalicylate drugs / Anti-TNF therapy Monoclonal antibodies Abatacept /
Proton pump inhibitors / Sildenafil Anaesthetic drugs / Inhaled anaesthetic-like agent
Pseudocholinesterase deficiency Succinyl choline Local
spinal anesthetics / Fentanyl Ketamine / Topoisomerase inhibitors

itamin C (ascorbic acid) (scurvy) Vitamin B12 deficiency Vitamin
B1 (Thiamine) deficiency Vitamin E deficiency Vitamin K
Deficiency / Vitamin A deficiency Vitamin deficiency Zinc deficiency /
Pyruvate kinase

Chapter 15 Immunology Human leukocyte antigen (HLA) Cluster of Differentiation (CD
Markers) Complement pathways Anaphylaxis
..... Exercised induced anaphylaxis Anaphylactic
reactions associated with anaesthesia Allergy tests Latex allergy
..... Serum Sickness Immune system
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atherosclerosis Fibroblasts / Immunoglobulins Protein analysis:
Gamma globulins Immunoglobulins: therapeutics Leukotrienes / Acute
phase proteins ANCA / Antibodies and immunological markers Interleukins
..... Interferon Tumour necrosis
factor (TNF) Chapter 16 Genetics Autosomal dominant conditions
Achondroplasia Osteogenesis imperfecta (“brittle bone disease”)
Down’s syndrome (trisomy 21) Noonan’s syndrome
Ehlers–Danlos syndrome (EDS) Pseudoxanthoma elasticum (PXE)
Phenylketonuria (PKU) Alkaptonuria X-
linked recessive X-linked dominant disorders Vitamin
D-resistant rickets Mitochondrial diseases Kearns-Sayre
syndrome Kallman’s syndrome Klinefelter’s syndrome
..... Turner’s syndrome

Nitric oxide (NO) Endothelin-1 (ET-1) / Kinins Erythrocyte sedimentation rate (ESR) Leukocyte alkaline phosphatase Thymus / B cells (B lymphocytes) T cells (T lymphocytes) Primary immunodeficiency Selective IgA deficiency IgG subclass deficiency Isolated IgD deficiency Common variable immunodeficiency (CVID) Bruton's agammaglobulinemia (X-linked agammaglobulinemia) Severe combined immunodeficiency disease (SCID) DiGeorge syndrome Wiskott-Aldrich syndrome (WAS) Complement deficiencies Hereditary angioedema Granulomatous inflammation

Marfan's syndrome Homocystinuria Fragile X syndrome Trinucleotide repeat disorders / Genetic anticipation Polygenic diseases Lysosomal storage diseases /Gaucher's disease Fabry's disease Mucopolysaccharidoses (MPS) Glycogen storage disorders (GSD) McArdle's disease Linkage disequilibrium / Imprinting Prader-Willi syndrome Angelman syndrome / Mutations Chromosome abnormality McCune-Albright syndrome (MAS)

Chapter 17 Genetics Significance tests The power Significance tests: types Choosing the appropriate test Normal distribution Standard deviation Skewed distributions Confidence interval and standard error of the mean Confounding variable Correlation and linear regression Correlation coefficient / Screening test statistics Incidence and prevalence Relative risk Numbers needed to treat and absolute risk reduction Odds and odds ratio Pre- and post- test odds and probability Screening: Wilson and Junger criteria Scales of measurement Systematic review (meta-analysis) Randomised controlled trial (RCT) Case-control study / Cohort study Observational study / Biological assays Sequential trial / Crossover trial Sampling / Bias (Systematic error) Study design: evidence and recommendations Study design: new drugs Graphical representation of data

Third edition Notes & Notes For MRCP part 1 & 2 By Dr. Yousif Abdallah Hamad Rheumatology Updated 2022

Chapter 8

Rheumatology

Bone markers Bone remodeling • Cells involved □ Osteoclasts: degrade bone tissue by secreting collagenase and H⁺ □ Osteoblasts: □ Build bone tissue by secreting type I collagen □ Activity assessed by an increase in bone ALP, osteocalcin, and type I procollagen propeptides Bone markers are useful for: • prediction of prognosis • prediction of fracture risk • assessing suitability for

therapy and • monitoring the success of therapy. Markers of bone formation (measured in serum) • Bone-derived alkaline phosphatase (ALP). • Osteocalcin • Procollagen type 1 propeptides. • Hydroxyproline.

Rheumatoid factor Overview • Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG. • Rheumatoid factor is an antibody with reactivity to the heavy chain of IgG. • The rheumatoid factor may be of IgM, IgG or IgA class. • The conventional (agglutination) test, detects only IgM RF. • high titre levels are associated with severe progressive disease (but NOT a marker of disease activity). A positive rheumatoid factor is associated with: • More severe erosive disease • Extra-articular manifestations including subcutaneous nodules and • Increased mortality. Conditions associated with a positive RF include: • Sjogren's syndrome (around 100%) • Felty's syndrome (around 100%) • Mixed cryoglobulinemia (types II and III) - 40 to 100% Notes & Notes for MRCP

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Markers of bone resorption (measurable in serum or urine) • Telopeptides • Pyridinium cross-linking molecules • Tartrate-resistant acid phosphatase (TRAP)

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• rheumatoid arthritis (70-80%) • Mixed connective tissue disease - 50 to 60% • infective endocarditis (= 50%) • SLE (= 20-30%) • systemic sclerosis (= 30%) • Polymyositis/dermatomyositis - 5 to 10% • general population (= 5%)

Rheumatoid arthritis • Around 70% of patients with rheumatoid arthritis are HLA-DR4. • Patients with Felty's syndrome (a triad of rheumatoid arthritis, splenomegaly and neutropaenia) are even more strongly associated with 90% being HLA-DR4 Epidemiology • Prevalence = 1% • F:M ratio = 3:1 • Peak onset = 30-50 years, although occurs in all age groups Aetiology • Idiopathic inflammatory autoimmune disorder of unknown etiology • Genetic disposition: associated with HLA-DR4 and HLA-DR1 Pathophysiology • Autoimmune — inflammation induces formation of pannus (proliferative granulation tissue), which erodes articular cartilage and bone. • Citrullinated proteins (converted from arginine to citrulline) are recognized as foreign → Activation and migration of CD4+ T cells to synovial joints → recruitment of macrophages → secretion of cytokines (TNF- α , IL-1, IL-6) → inflammation and proliferation → pannus and synovial hypertrophy → invasion, progressive destruction, and deterioration of cartilage and bone • TNF is an important in the pathogenesis of rheumatoid arthritis. • Rheumatoid factor (RF) □ Antibodies against Fc portion of IgG (rheumatoid factor, RF) are produced to aid in removing autoantibodies and immune complexes. □ RF excess triggers formation of new immune complexes and type III hypersensitivity reaction □ Individuals with positive RF are more likely to develop extraarticular manifestations. Rheumatoid arthritis - TNF is key in pathophysiology Diagnosis • The diagnosis of RA is clinical

Chapter 8

Rheumatology

• NICE have stated that clinical diagnosis is more important than criteria such as those defined by the American College of Rheumatology. • Consider RA in patients with arthralgia, joint stiffness, and synovitis lasting ≥ 6 weeks 2010 American College of Rheumatology criteria • Target population. Patients who:

1. have at least 1 joint with definite clinical synovitis
2. with the synovitis not better explained by another disease • Classification criteria for rheumatoid arthritis (add score of categories A-D; a score of 6/10 is needed definite rheumatoid arthritis) Factor A. Joint involvement B. Serology (at least 1 test result is needed for classification) C. Acute-phase reactants (at least 1 test result is needed for classification) D. Duration of symptoms Notes & Notes for MRCP
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Scoring 1 large joint

2 - 10 large joints

1 - 3 small joints (with or without involvement of large joints)

4 - 10 small joints (with or without involvement of large joints)

10 joints (at least 1 small joint)

Negative rheumatoid factor (RF) and negative anti-cyclic citrullinated peptide (Anti-CCP)

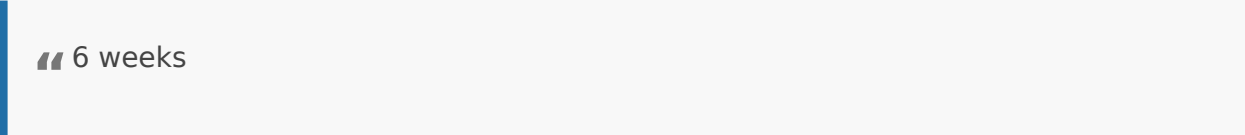
Low-positive RF or low-positive Anti-CCP

High-positive RF or high-positive Anti-CCP

Normal CRP and normal ESR

Abnormal CRP or abnormal ESR

< 6 weeks



6 weeks

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Articular manifestations • Polyarthralgia □ Symmetrical pain and swelling of affected joints (also at rest) □ Frequently affected joints □ Metacarpophalangeal (MCP) joints □ Proximal interphalangeal (PIP) joints (DIP joints are NOT typically affected in RA.) □ Wrist joints • Morning stiffness (often > 30 min) that usually improves with activity • Joint deformities □ Swan neck deformity: PIP hyperextension and DIP flexion □ Boutonniere deformity: PIP flexion and DIP hyperextension. □

Hitchhiker thumb deformity (Z deformity of the thumb): hyperextension of the interphalangeal joint with fixed flexion of the MCP joint □ Ulnar deviation of the fingers □ Piano key sign: dorsal subluxation of the ulna □ Atlanto-axial subluxation: A loss of ligamentous stability between the atlas (C1) and axis (C2), which can result in compression of the spinal cord, medulla, and/or vertebral arteries by the odontoid process, especially upon neck flexion. Most commonly caused by Down syndrome, rheumatoid arthritis, and trauma. The earliest manifestation of rheumatoid arthritis in the feet → swelling of the metatarsophalangeal joints Extraarticular manifestations • Constitutional symptoms: Low-grade fever, myalgia, malaise, fatigue, weight loss • Rheumatoid nodules: □ Nontender, firm, subcutaneous swellings (2 mm–5 cm). Commonly occur in areas exposed to higher pressure, e.g., extensor side of the forearm, bony prominences □ Rheumatoid pulmonary nodules may be accompanied by fibrosis and pneumoconiosis (Caplan syndrome). □ • Lungs: □ pleuritis, pleural effusions, interstitial lung disease (e.g., organizing pneumonia) □ rheumatoid pleural effusion: characterised by →low glucose level □ cricoarytenoid arthritis:

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Rheumatology □ seen in up to 75% of patients with RA □ It can cause stridor, but is often asymptomatic. □ symptoms can rapidly worsen in the post-operative period. □ the most helpful diagnostic test →Spirometry with flow-volume loop □ Patients can need urgent tracheostomy and steroids, both orally and via joint injection. • Eye: □ keratoconjunctivitis sicca (dry eyes) (most common) □ scleritis, and episcleritis • Endocrine and exocrine glands: secondary Sjogren syndrome • Hematological □ Anemia of chronic disease (normocytic anemia) □ NSAIDs and/or steroids → increased risk of GI bleeding → iron deficiency anemia (microcytic anemia) □ Methotrexate → decreased folate level → macrocytic anemia □ Neutropenia □ Splenomegaly • Heart: □ Pericarditis and myocarditis, constrictive pericarditis is the commonest cardiac complication of rheumatoid arthritis □ ↑↑ risk of myocardial infarction, stroke. • Musculoskeletal: Tenosynovitis and bursitis, Carpal tunnel syndrome • Vascular: □ Peripheral vasculitis, manifests as livedo reticularis □ Raynaud phenomenon Investigations Anti-cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis • Specific parameters (serological studies) □ Anti-cyclic citrullinated peptide (Anti-CCP) antibodies □ It has sensitivity similar to RF (70-80%) with a much higher specificity of 90-95%. □ a prognostic marker. □ Rheumatoid factor (RF) □ IgM autoantibodies against the Fc region of IgG antibodies □ Present in 70-80% of patients, but not specific to RA □ Serological studies may be negative (i.e., seronegative RA): Up to 30% of patients with RA are negative for Anti-CCP and RF. • Radiographic features □ X-ray of both hands and feet: initial test □ Early findings : soft tissue swelling, osteopenia (juxta-articular) □ Late findings: joint space narrowing, marginal erosions of cartilage and bone, osteopenia (generalized), subchondral cysts • Typical RA findings on x-rays may be subtle or absent upon diagnosis in many patients with early RA; therefore, ultrasound or MRI may be more informative, as they have higher sensitivity for detecting early signs of inflammation and erosion. • Analysis of synovial fluid □ Sterile specimen with leukocytosis (WBC count 5000–50,000/mcL) □ Abundant neutrophils. □ High protein levels.

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The radiographic features of rheumatoid arthritis can be remembered by the mnemonic LESS: Loss of joint space, Erosions, Soft tissue swelling, and Soft bones (osteopenia) Early x-ray findings Late x-ray findings • loss of joint space • juxta-articular osteoporosis • soft-tissue swelling • periarticular erosions • subluxation Differential diagnosis • Rheumatoid arthritis typically affects the metacarpophalangeal and proximal interphalangeal joints symmetrically. Psoriatic arthritis affects the distal interphalangeal joints and tends to be asymmetrical. • Rheumatoid arthritis vs osteoarthritis Rheumatoid arthritis Osteoarthritis pathophysiology autoimmune (inflammatory) degenerative due to ↑ wear and tear on joints □ loss of cartilage (noninflammatory) Age of starting At any age Usually later in life Speed of onset Rapid, over weeks to months Slow, over years Pain improves with movement worse with movement and better with rest Primary joint affected Proximal interphalangeal Distal interphalangeal Metacarpophalangeal Carpometacarpal Heberdens nodes Absent Present Joint characteristics Soft, warm and tender Hard and bony (little or no swelling) Stiffness Worse after resting (morning stiffness) If present, worse after effort, may be described as evening stiffness Usually > 1 hour Usually < 1 hour Systemic symptoms Present (eg: fatigue) Absent RF and anti-CCP Positive Negative ESR and Creactive protein Elevated Normal x-ray Osteophytes absent Osteophytes may be present

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Rheumatology Referral • Indications for urgent referral for specialist opinion: any person with suspected persistent synovitis of undetermined cause. Refer urgently if any of the following apply: □ the small joints of the hands or feet are affected □ more than one joint is affected □ there has been a delay of 3 months or longer between onset of symptoms and seeking medical advice.

Prognosis: poor prognostic features:

- Anti-CCP antibodies (The poorest prognostic factor) • Rheumatoid factor positive • HLA DR4 • Insidious onset : Acute or Sudden onset is not a poor prognosis. • Poor functional status at presentation • X-ray: early articular erosions (e.g. within the first 6 months of presentation and in less than < 2 years) • Extra articular features e.g. nodules • Female sex. Which micro-organisms may be associated with the development of rheumatoid arthritis in susceptible patients? →Proteus mirabilis Felty's syndrome (RA + splenomegaly + low white cell count) Poorly controlled rheumatoid arthritis + proteinuria and hypoalbuminaemia raises the possibility of systemic amyloidosis → Rectal biopsy MRCPUK-part-1-September- 2009 exam: MRCPUK-part-1-jan-2018: Which (HLA) types is most associated with rheumatoid arthritis? □ HLA DR4

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By Dr. Yousif Abdallah Hamad

A patient of RA on etanercept, scheduled for elective surgery. What advice regarding his medication should be given prior to surgery? □ Stop etanercept 2–4 weeks prior to surgery Updated British Society for Rheumatology (BSR) guidelines (January 2005) for prescribing tumour necrosis factor (TNF-α) blockers in adults with RA recommend: • withholding etanercept and other TNF-blockers (infliximab and adalimumab) for 2–4 weeks prior to a major surgical procedure. • restarted postoperatively if there is no evidence of infection and once wound healing is satisfactory.

Rheumatoid arthritis: Management Approach • Acute anti-inflammatory treatment □ Temporary (< 3 months) symptomatic treatment with glucocorticoids and/or NSAIDs is indicated for disease flares (i.e., episodes of increased disease activity and symptom worsening). □ Glucocorticoids (prednisone) □ Short-term (i.e., < 3 months) therapy at the lowest effective dose is preferred. □ Longer term therapy only used in patients with highly active RA who do not respond to maximum doses of DMARDs. □ Glucocorticoids should be used at the lowest effective dose and only for short periods of time to reduce the risk of their many adverse effects (e.g., hypertension, osteoporosis, infections). □ NSAIDs and selective COX-2 inhibitors: relieve symptoms, but do not improve the prognosis. • Long-term treatment □ Initiation of treatment: all patients with evidence of joint inflammation should start a combination of disease-modifying drugs (DMARD) as soon as possible. □ Consider short-term concomitant use of acute anti-inflammatory therapy (i.e., glucocorticoids and/or NSAIDs) for symptom control until the onset of action of DMARDs (e.g., ≥ 6 weeks). Disease-modifying anti-rheumatic drugs (DMARDs) • DMARD therapy reduces RA mortality and morbidity by up to 30%. • If DMARD therapy induce disease control → reduce drug doses to levels that still maintain disease control. • Methotrexate (MTX) □ first-line treatment in patients with moderate to high disease activity □ All patients should be co-prescribed folic acid supplementation at a minimal dose of 5 mg once weekly to minimize adverse effects. □ Monitoring of FBC & LFTs is essential due to the risk of myelosuppression and liver cirrhosis. □ Other important side-effects include pneumonitis • Azathioprine (AZA) □ Patients should have baseline thio-purine methyl-transferase (TPMT) status assessed • Sulfasalazine □ Consider in patients with low disease activity if MTX is contraindicated, e.g., during pregnancy.

Notes & Notes for MRCP

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Rheumatology

□ Adverse effects: diarrhea, agranulocytosis, cutaneous hypersensitivity reactions • Hydroxychloroquine (HCQ) □ Consider in patients with low disease activity. □ Adverse effects: hyperpigmentation and retinopathy □ Patients should have baseline formal ophthalmic examination, ideally including objective retinal assessment for example using optical coherence tomography, within 1 year of commencing an antimalarial drug • Leflunomide □ Consider if all other conventional DMARDs are contraindicated. □ Mechanism of action: reversibly inhibits dihydroorotate dehydrogenase → impaired pyrimidine synthesis → inhibition of T-cell proliferation □ Other indications: psoriatic arthritis Monitoring rheumatoid arthritis • Recommended DMARD Blood Monitoring Schedule when Starting or Adding a New DMARD (BSR guidelines February 2017) □ Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin □ every 2 weeks until on stable dose for 6 weeks; □ then once on stable dose, monthly for 3 months; □ thereafter, at least every 12 weeks. □ Contact rheumatology team urgently and consider interruption in treatment if any of the following develop: □ white cell count $<3.5 \times 10^9/l$; □ mean cell volume >105 fL; □ neutrophils $<1.6 \times 10^9/l$; □ creatinine increase $>30\%$ over 12 months and/or calculated GFR <60 ml/min; □ unexplained eosinophilia $>0.5 \times 10^9/l$; □ ALT and/or AST >100 U/l; □ platelet count $<140 \times 10^9/l$; □ unexplained reduction in albumin <30 g/l □ In the setting of acute infection, most DMARDs (except hydroxychloroquine) should be discontinued until the infectious process has resolved. • Measure CRP and key components of disease activity (using a composite score such as DAS28)

regularly (monthly until treatment has controlled the disease) to inform decision-making about: □ increasing treatment to control disease □ cautiously decreasing treatment when disease is controlled. The first-line treatment for newly diagnosed active RA → combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids) as soon as possible, ideally within 3 months of the onset of persistent symptoms. TNF-inhibitor • The current indication for a TNF-inhibitor is an inadequate response to at least two DMARDs including methotrexate • Examples of anti-TNF alpha agents: □ Etanercept: SC administration twice weekly □ Infliximab: IV administration □ Adalimumab: SC administration • Adverse effects of TNF blockers include: □ reactivation of latent tuberculosis and demyelination. □ The risk of TB reactivation is most pronounced in the first 3 months of treatment.

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□ BTS guidelines therefore recommend a clinical examination, and chest radiograph to check for TB. □ In the UK, patients have a baseline CXR and assessment of risk of infection with *Mycobacterium tuberculosis* prior to starting treatment with anti-TNF α . • Any patient with active TB, □ should receive standard chemotherapy. □ They must complete two months full treatment before starting anti-TNF alpha treatment. • Patients with past TB, □ who have received previous adequate therapy □ can be started on anti-TNF alpha therapy but need to be monitored regularly. □ TB not previously adequately treated, □ chemoprophylaxis should be given before commencing anti-TNF alpha treatment. □ What is the optimal TB screening test in patient with previous TB? □ Interferon gamma release assay □ The test is not altered by previous TB or previous BCG vaccination. □ Positive testing indicates a need for anti-tuberculous treatment alongside golimumab, for example isoniazid. □ Mantoux testing is less indicative of prior infection because it is likely to evoke a positive reaction in patients with previous TB or who have received BCG vaccination. • Patients with a normal chest radiograph who have not started immunosuppressive therapy → a tuberculin test is helpful. • Patients with a normal chest radiograph + already on immunosuppressive treatment, □ the result of the tuberculin test is dampened and it is therefore not useful. □ An individual risk assessment should be made: if the annual risk of TB is greater than that of drug-induced hepatitis then chemoprophylaxis should be given. If not, the patient should be monitored and investigated early if symptoms consistent with TB develop. □ Chemoprophylaxis is generally with isoniazid for 6 months. • Patients who test positive with either of Quantiferon Gold test and Elispot tests should be treated with chemoprophylaxis (either isoniazid for 6 months, or dual therapy Rifampicin + INH for 2 months) at the same time as being started on anti-TNF alpha treatment. • TNF-inhibitors should be stopped 2-4 wks before any major operation. Rituximab • Action □ Anti-CD20 monoclonal antibody, results in B-cell depletion. • Prescription □ Two doses of 1g intravenous infusions are given two weeks apart. • Indications □ rheumatoid arthritis □ Nice guidelines of RA □ Rituximab in combination with methotrexate is recommended as an option for treatment of rheumatoid arthritis who have had an inadequate response to or intolerance of other disease-modifying antirheumatic drugs (DMARDs), including treatment with at least one tumour necrosis factor α (TNF- α) inhibitor therapy. □ non-Hodgkin lymphoma (The primary clinical use) □ idiopathic thrombocytopenic purpura. • Follow up □ Treatment with rituximab plus methotrexate should be continued only if: □ There is an adequate response following initiation of therapy. □ An adequate response is defined as an improvement in disease activity score

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