UNIT NO. 1

APPROACH TO SYMMETRICAL POLYARTHRITIS WITH FOCUS ON RHEUMATOID ARTHRITIS

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ABSTRACT

Symmetrical polyarthritis is not uncommon as a presenting clinical problem in the primary care setting. The ability to differentiate inflammatory from non-inflammatory, articular from peri-articular joint pain will help the Family Physician (FP) to further narrow the diagnosis of joint pain, and provide early referral and effective treatment when necessary. Integrating clinical reasoning with the concept of likelihood ratios in the process of diagnosis, FPs can also easily differentiate the various diagnoses of symmetrical polyarthritis, including rheumatoid arthritis (RA). There is also increasing evidence that shared care of patients with rheumatoid arthritis can be done successfully and safely between FPs and rheumatologists.

Keywords: Symmetrical Polyarthritis; Rheumatoid Arthritis; Likelihood Ratios; Shared Care;

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INTRODUCTION

Joint pain is one of the top ten common chief complaints in the Family Physician (FP) setting. The ability to differentiate inflammatory from non-inflammatory, articular from peri-articular joint pain will help the FP to further narrow the diagnosis, and provide early referral and effective treatment when necessary. This article aims to achieve the following learning outcomes:

1. Apply the "RIME model" (Reporter, Interpreter, Manager, Educator) framework within the context of a clinical approach to joint pain.
2. Differentiate inflammatory from non-inflammatory, articular from peri-articular joint pain from a medical science perspective.
3. Integrate clinical reasoning with evidence-based medicine in the various diagnoses of symmetrical polyarthritis.
4. Perform shared care of rheumatoid arthritis patients with a rheumatologist.

THE ROLE OF THE "REPORTER"

In the RIME (Reporter, Interpreter, Manager, Educator) framework,[1] the "reporter" represents the most critical stage, because the asking of appropriate questions to describe the patient and differentiate the diagnosis will form the key determinants of patient management. A typical example of a question that describes the patient is the "pain score", which does not help much in differentiating the diagnosis, but is of vital importance to the patient. An example of a question that differentiates the diagnosis will be the symptom and sign of "podagra", which is more likely in a patient with acute gouty arthritis. Questions that differentiate the diagnosis well, will inform "what is the matter with the patient". An accurate diagnosis is the cornerstone of good clinical care. Questions that help to describe the patient well, will inform "what really matters to the patient", and therefore allow the physician to craft a care plan that meets the expectations, culture, and values of the patient. This will also ensure better patient acceptance and compliance with the care plan. The ability of asking the right questions to describe the patient and differentiate the diagnosis, respectively, will be the essential skills of a good "reporter".

Clinical Application of Medical Science Knowledge

By applying the knowledge of pathophysiology, inflammatory from non-inflammatory joint pain can be differentiated (see Table 1).

Table 1: Differences between inflammatory from non-inflammatory joint pain.

	Inflammatory	Non-inflammatory
Signs	Swollen, red, warm	Usually not swollen, red, warm
Early Morning stiffness	More than 1 hour	Less than 30 minutes
Movement	Pain relieved by movement and worsened by rest	Pain worsened by movement and relieved by rest

Likewise, articular from peri-articular joint pain can also be differentiated (see Table 2).

Table 2: Differences between articular and peri-articular joint pain.

	Articular	Periarticular
Movement	Passive and active movements are both painful	Passive movement is less painful than active movement
Tenderness	Tender along joint line	Tender at structure of involvement
Planes of movement	Pain in all planes of joint movement	Pain in certain planes of movement, stress test positive

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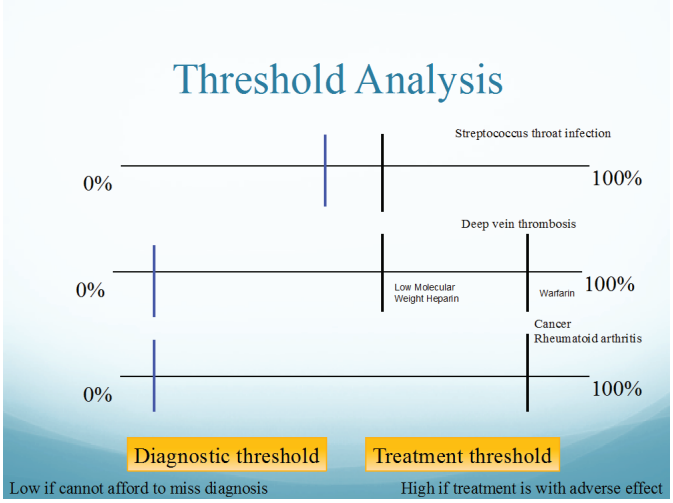
THE PROCESS OF DIAGNOSIS

Medical diagnosis is a probabilistic science. In other words, FPs often estimate the probability of a particular diagnosis after taking a patient's history and performing a physical examination. Thereafter, appropriate laboratory tests or radiographic imaging are ordered when needed to further "rule in" or "rule out" a diagnosis. Two thresholds are often considered in the process: the "diagnostic threshold" which is defined as the probability below which the diagnosis warrants no further consideration and the "treatment threshold" which is defined as the probability above which the diagnosis is sufficiently likely to warrant therapy. Different medical conditions will have different probability thresholds for diagnosis versus treatment. A condition that is not serious and can allow for time to evolve or resolve it further, will usually have a high "treatment threshold". A condition for which the treatment is safe and inexpensive, may have a low "diagnostic threshold" (Figure 1). It is only when the probability of a particular condition falls between the diagnostic and treatment thresholds that investigations will be required, so that the negative or positive results of the tests can further rule in (when positive) or rule out (when negative) the condition. [2]

Figure 1. Threshold analysis.



The saying that "90% of clinical diagnosis can be made with a good history and physical examination" stems from the fact that every symptom or sign is also useful to "rule in" or "rule out" a diagnosis.[3] In evidence-based medicine appraisal of diagnostic tests, the "SPin" and "SNout" rules are useful. A highly sensitive test (may be a symptom, sign or laboratory test), when negative, rules out a diagnosis (SNout) and a highly specific test, when positive, rules in a diagnosis (SPin). Another similar approach is the use of the concept of "likelihood ratio" (LR). LRs simply compare two likelihoods—the frequency of a test result in those with the target disorder compared to the frequency of the same test result in those without the disease. An easy way to apply LR in a clinical setting is shown in Table 3. Simply put, to confirm a diagnosis, look out for symptoms, signs or tests with high LR when the symptoms, signs or test are positive. To exclude a diagnosis, look out for symptoms, signs or tests with low LR when the symptoms, signs or test are negative.

Table 3: How to apply Likelihood Ratios in a clinical setting.[4]

Likelihood ratio	Change in probability	Effect on disease
10	45%	Large
5	30%	Moderate
2	15%	Slight
1	0	None
0.5	-15%	Slight
0.2	-30%	Moderate
0.1	-45%	large

One simple example of the elegance of such an approach to the process of diagnosis is gouty arthritis. Referring to Table 4 below, the presence of podagral (symptom/ sign), rapid onset of pain and swelling (symptom), tophi (sign) and erythema (sign) are all associated with LR+ values of greater than 5. Therefore the diagnosis of gouty arthritis will be more likely when these symptoms and/or signs are present.[5]

Table 4: CGD proposal, diagnostic value.

CGD items	Sensitivity	Specificity	LR+	LR−
1. >1 arthritis attack	94.6 (88.8–97.5)	33.7 (24.9–43.8)	1.4 (1.2–1.6)	0.16 (0.07–0.36)
2. Mono/oligoarthritis	97.3 (92.4–99.1)	67.4 (57.3–76.1)	2.98 (2.2–4.0)	0.04 (0.01–0.12)
3. Rapid onset of pain and swelling (<24 h)	82.5 (79.4–88.3)	98.9 (94.2–99.8)	77.5 (11.0–545.5)	0.18 (0.12–0.26)
4. Podagra	71.4 (62.5–79)	90.2 (82.4–94.8)	7.30 (3.8–13.7)	0.32 (0.23–0.43)
5. Erythema	70.5 (61.5–78.2)	97.8 (92.4–99.4)	32.4 (8.2–128.4)	0.30 (0.23–0.40)
6. Tarsitis	31.3 (23.4–40.3)	85.9 (77.3–91.6)	2.21 (1.2–3.9)	0.80 (0.68–0.95)
7. Probable tophi	67.9 (88.7–75.8)	98.9 (94.1–99.8)	62.43 (8.8–440.3)	0.32 (0.25–0.43)
8. Hyperuricemia	98.2 (93.7–99.5)	86.8 (78.4–92.3)	7.45 (4.3–12.6)	0.02 (0.01–0.08)
≥3 items	99.1 (95.2–99.8)	79.8 (70.6–86.7)	4.90 (3.28–7.33)	0.01 (0.00–0.08)
≥4 items	97.3 (90.8–99.3)	95.6 (89.2–98.3)	22.1 (8.4–57.7)	0.03 (0.01–0.11)
≥5 items	83.9 (76.0–89.6)	96.7 (90.8–98.9)	25.7 (8.4–78.5)	0.17 (0.11–0.25)

In parentheses: 95% confidence intervals

Adapted from "The diagnostic value of the proposal for clinical gout diagnosis"[5]

Approach to Symmetrical Polyarthritis

For a patient who presents with symmetrical polyarthritis involving the small and large joints, the following four conditions are possible differential diagnoses: Rheumatoid Arthritis (RA), Sjogren Syndrome (SS), Systemic Lupus Erythematosus (SLE), and Psoriatic Arthritis (PsA).

Using the process of diagnosis based on the likelihood ratio approach, the old criteria of the American College of Rheumatology (1987)[6] and anti-citrullinated peptide auto-antibodies test can help FPs to effectively diagnose RA patients (Table 5).[7,8] Fewer than 4 of the old classification criteria (1987)[6] and negative anti-citrullinated peptide autoantibodies would exclude rheumatoid arthritis. Even if a patient did not have sufficient probability of disease (below 4 of the old criteria), but the anti-citrullinated peptide autoantibodies were highly positive, a diagnosis of rheumatoid arthritis should still be

considered.[9]

In the same manner, this process of diagnosis using likelihood ratios can be applied to the other conditions that present as symmetrical polyarthritis: Sjogren Syndrome (SS; Table 6),[10] Systemic Lupus Erythematosus (SLE; Table 7),[11] and Psoriatic Arthitis (PsA; Table 8).[12]

Table 5: Revised American Rheumatism Association criteria for classification of Rheumatoid Arthritis.

SIGN OR SYMPTOM	DEFINITION	LR+	LR-	PERCENTAGE WITH RHEUMATOID ARTHRITIS IF SIGN OR SYMPTOM IS*:	
				PRESENT	ABSENT
Morning stiffness	Stiffness in or around the affected joints for at least one hour after initiating movement	1.9	0.5	39	14
Arthritis of three or more joint areas	Three or more of the following joints noted to be fluid-filled or have soft tissue swelling: wrist, PIP, MCP, elbow, knee, ankle, MTP	1.4	0.5	32	13
Hand joint involvement	Wrist, MCP, or PIP joints among the symptomatic joints observed	1.5	0.4	33	12
Symmetric arthritis	Right and left joints involved for one or more of following: wrist, PIP, MCP, elbow, knee, ankle, MTP†	1.2	0.6	29	17
Rheumatoid nodules	Subcutaneous nodules in regions surrounding joints, extensor surfaces, or bony prominences	3.0	0.98	50	25
Serum rheumatoid factor positive	Positive result using any laboratory test that has a positive predictive value of 95 percent or more (i.e., is positive in no more	8.4	0.4	74	13

Table 6: Diagnostic performance of individual features for established Sjogren Syndrome patients.

	Positive (*n*)	Negative (*n*)	No known (*n*)	Sensitivity	Specificity	PPV	LR^+
Ocular symptoms	78	19	2	0.80	0.19	0.64	0.99
Oral symptoms	75	22	2	0.77	0.14	0.62	0.90
Ocular signs	90	6	3	0.94	0.20	0.64	0.95
Salivary gland involvement	4	5	90	–	–	–	–
Histopathology							
Chisholm's score (III/IV)	78	21	0	0.79	1.00	1.00	–
Autoantibodies (the least one positive)	51	46	2	0.53	0.75	0.80	2.10
Anti-nuclear antibody(+)	39	57	3	0.41	0.87	0.85	3.10
Ig M rheumatoid factor(+)	25	66	8	0.27	0.90	0.93	2.70
Anti-Ro(+)	13	61	25	0.18	0.95	0.87	3.60
Anti-La(+)	6	66	27	0.80	0.93	0.67	1.10
Lymphopenia	19	72	8	0.21	0.92	0.83	2.60
Raynaud's phenomenon	17	77	5	0.18	0.94	0.85	3.00
Arthralgia or arthritis	58	35	7	0.62	0.35	0.63	0.95
Hypergammaglobulinemia	11	56	22	0.17	–	–	–

Likelihood ratio$^+$ ($LR^{+)}$ = Sensitivity/(1 − specificity)

PPV Positive predictive value

Table 7. Diagnostic performance of individual features for established SLE patients seen in academic referral centres.

Feature	Sensitivity	Specificity	LR+	LR-
Rash (photosensitive/malar/ACLE)	65%	80%	3.3	0.43
Discoid rash	20%	94%	3.1	0.86
Oral ulcers	44%	92%	5.6	0.61
Non-scarring alopecia	32%	96%	7.4	0.71
Arthritis	79%	44%	1.4	0.48
Serositis	35%	97%	12.6	0.67
Renal	33%	96%	9.1	0.70
Neurologic	6%	99%	5.5	0.95
Haemolytic anaemia	7%	100%	14.2	0.93
Leukopenia	46%	95%	8.9	0.57
Lymphopenia <1500	49%	82%	2.7	0.63
Lymphopenia <1000	17%	95%	3.2	0.88
Thrombocytopenia	14%	98%	6.7	0.88
ANA	97%	45%	1.8	0.08
anti-dsDNA	57%	96%	13.9	0.45
Anti-Sm	26%	99%	20.1	0.75
aPL	54%	86%	3.8	0.54
Low complement	59%	93%	8.0	0.44

Table 8: The Classification Criteria for Psoriatic Arthritis (CASPAR)

CASPAR consists of established inflammatory articular disease with at least 3 points from the following features.

- Current psoriasis (assigned a score of 2)
- A history of psoriasis (in the absence of current psoriasis; assigned a score of 1)
- A family history of psoriasis (in the absence of current psoriasis and history of psoriasis; assigned a score of 1)
- Dactylitis (assigned a score of 1)
- Juxta-articular new-bone formation (assigned a score of 1)
- RF negativity (assigned a score of 1)
- Nail dystrophy (assigned a score of 1)

The CASPAR is regarded as being highly specific (99.1%) for the diagnosis of PsA, however the sensitivity for detecting early PsA was found to be much lower, 87.4. [12] This will convert to a LR+ of 97.1 and LR- of 0.13.

Principles of Care for Rheumatoid Arthritis Patients

The core principles of care for RA patients are:

Core principle 1
Detect and refer patients early, even if the differential diagnosis is uncertain. While the differential diagnosis can prove difficult in early RA, 3 simple and effective criteria could be included in shared care protocols to encourage appropriate referral by FPs:[13] 3 or more objectively swollen joints on examination; morning stiffness lasting > 30 min; and involvement of the metacarpal–phalangeal or metatarsal– phalangeal joints, or both (squeeze test positive).

Core principle 2
Treat RA immediately.

Core principle 3
Tight control of inflammation in RA improves outcomes, and requires structured protocols and regular review.

Core principle 4

Consider the risk–benefit ratio and tailor treatment to each patient.

Key recommendation 1: Increase awareness among the public and professionals.

Key recommendation 2: Create systems to ensure early diagnosis and treatment.

Key recommendation 3: Titrate treatment regularly depending on disease activity.[14]

Studies in Denmark and Singapore have shown that the follow-up care regime for outpatients with RA can be changed from a traditional rheumatologist's setting to tight follow-up with nursing consultations or shared care with FPs without a decline in disease control. [15,16]

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LEARNING POINTS

- **By differentiating inflammatory from non-inflammatory, articular from peri-articular joint pain, Family Physicians (FPs) can narrow the diagnosis of joint pain, and provide early referral, and effective treatment when appropriate**
- **By Integrating clinical reasoning with the concept of likelihood ratios in the process of diagnosis, FPs can readily differentiate the various diagnosis of symmetrical polyarthritis, including rheumatoid arthritis.**
- **Shared care of patients with rheumatoid arthritis can be done successfully and safely between FPs and rheumatologists.**