Summer SCHOOL 2025

*A residential learning experience*

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Novotel Geelong, VIC

# The High-Risk Foot Beyond Diabetes. A rheumatology perspective

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# The Clinical Dilemma – the red hot swollen foot

- 50 year old man with a history of gout, last uric acid measure 5.4mg/dL
- Presents complaining of a flare in his arthritis at ankle / foot
- 2 day history of pain, redness, swelling
- Unable to bear weight
- Denies trauma, surgery or history of puncture
- Temperature of 38.5°c
- Resting pulse rate 90 beats per minute

Ankle / foot

- Warm to touch, erythematous
- swollen and tender on palpation
- Decreased ROM
- Antalgic gait

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# The Clinical Dilemma – the red hot swollen foot

- Is this active gout?
- Could this be septic arthritis?
- What is best practice guidance?
- How can we adapt best practice when working in a community setting?


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# Septic arthritis

Bacterial invasion of a synovial space
Yearly incidence 2 to 10 per 100,000 in general population[1]
Yearly incidence 30 to 70 per 100,000 in patients with RA and those with joint prosthesis[2]
Associated with significant mortality
In-hospital mortality figures of treated infections can be as high as 15%[3]
In-hospital mortality figures of RA patients as high as 50%[4,5]
Permanent disability and increased mortality associated with delayed presentations to clinic / diagnosis

Knee most common (50% cases)
Feet more common in diabetes and RA
Heamatogenous spread most common
Bacteria enter the synovial fluid easily as synovial tissue lacks a basement membrane

1. Margatten et al. 2007, JAMA; 297 (13): 1478-88. 2. Kaandorp et al. 1995, Arth Rheum; 38:1819-25. 3. Gupta et al. 2001; Rheumatology 40: 20: 24-30 2007. 4. Dubost et al. 1993 Medicine; 72: 296-310. 5. Goldenberg et al. 1985, N Engl J Med; 312: 764-771

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# Septic arthritis

Systematic review (2007)[1]

- Age > 80 years (+LR 3.5)[1]
- Diabetes mellitus (+LR 2.7)[1]
- Rheumatoid arthritis (+LR 3.5)[1] (twice as high in males)[2]
- Prosthetic joint (if overlying skin infection) +LR 15[1]
- Recent joint surgery within 3 months (+LR 3.5)
- Skin infection (+LR 2.8)
- Cutaneous ulcers
- IV drug use or recent catheterisation
- Alcoholism
- Previous intra-articular joint injection (1 per 100,000, 1 in 1666 if time 1-24 weeks considered)
- HIV and transplant

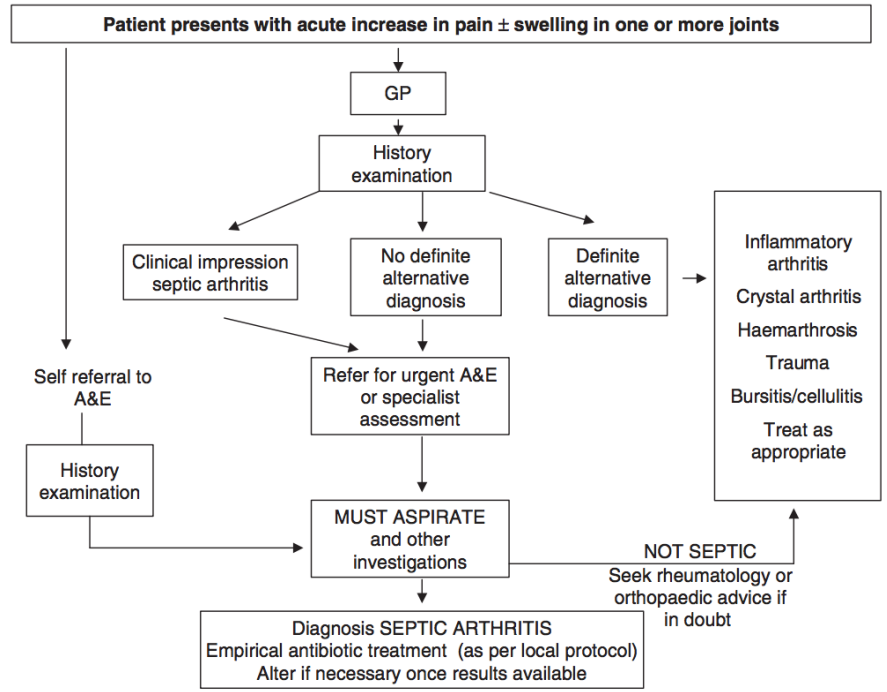
1. Margatten et al. 2007, JAMA; 297 (13): 1478-88. 2. Dubost et al. 1993 Medicine; 72: 296-310

# Septic arthritis

- Acute joint pain
- Swelling
- Warmth
- Erythema
- Can be subtle features in immunocompromised patients
- Fever > 38.5 (Sens. 46%  Spec 31%) Could miss 54% cases!
- Malaise
- Increased CRP >100 (Sens. 82-83%,  Spec. 27-70%)
- Increased ESR > 30 (Sens. 76-97%, Spec. 11-48%)
- Increased serum leukocyte count (>10,000 Sens 62-90%),
- (> 11,000, Sens. 75% Spec. 55%) – Could miss 25% cases!

*Symptoms and signs suggestive of septic arthritis*

(1) Patients with a short history of a hot, swollen and tender joint (or joints) with restriction of movement should be regarded as having septic arthritis until proven otherwise (B).
(2) If clinical suspicion is high, then it is imperative to treat as septic arthritis even in the absence of fever (B).




Carpenter et al. 2011 – Evidence based diagnostics: Adult septic arthritis Acad Emergency Med; 18:8:781-796

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# What happens in clinical practice

- ✓ Acute gout and septic arthritis are the two major diseases to consider in an acute monoarthritis
- ✓ Important to distinguish
  - Delay in septic arthritis poor outcome even fatal
  - Misled treatment – unnecessary surgical debridement
- ✓ Both cases joint aspiration invaluable

ORIGINAL PAPER
THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

**Poor adherence to guidelines on early management of acute hot swollen joint(s): an evaluation of clinical practice and implications for training**

Z. Farah,[1,*] V. Reddy,[2,3,*] W. Matthews,[4] I. Giles[2,3]

ORIGINAL ARTICLE
Immunology, Allergic Disorders & Rheumatology
JKMS
http://dx.doi.org/10.3346/jkms.2015.30.6.700 • J Korean Med Sci 2015; 30: 700-704

**Application of a Novel Diagnostic Rule in the Differential Diagnosis between Acute Gouty Arthritis and Septic Arthritis**

| Item | Score |
|---|---|
| Male | 2 |
| Previous patient reported arthritis attack | 2 |
| Onset within the day | 0.5 |
| Joint redness | 1 |
| 1st MTP joint involvement | 1.5 |
| Hypertension or at least 1 cardiovascular disease | 1.5 |
| Serum acid > 5.88mg/dL | 3.5 |

Score ≥ 8 – HIGH Probability of Gout
Score 4 and 8 – INTERMEDIATE
Score below 4 - LOW

Joint aspiration remains necessary to differentiate septic arthritis from another etiology.

Farah Z, Reddy V, Matthews W, Giles I. Poor adherence to guidelines on early management of acute hot swollen joint(s): an evaluation of clinical practice and implications for training. Int J Clin Pract. 2015 May;69(5):618-22. Lee KH, Choi ST, Lee SK, Lee JH, Yoon BY. Application of a Novel Diagnostic Rule in the Differential Diagnosis between Acute Gouty Arthritis and Septic Arthritis. J Korean Med Sci. 2015 Jun;30(6):700-4. Lafforgue A, Lambert C, Dubost JJ, Tournadre A, Soubrier M, Couderc M. Performance of a diagnostic score for gouty arthritis: results from a cohort of acute arthritis suspected of being septic. Rheumatol Int. 2023 Jan;43(1):119-124.

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# When evidence based practice is lacking !

Low levels of existing evidence
Complex and diverse cases

## Foot ulceration in Rheumatoid arthritis

| Factor | Facts & Figures | Level of Evidence |
|---|---|---|
| **Prevalence** | 10% with a history of ulceration<br>3.39% active ulceration in community setting[1]<br>4.37% ulceration over 3 year follow up[2] | 4 Large(ish) cross-sectional studies, two centres |
| **Incidence** | No published data | None |
| **Predictive factors** | Long disease duration[1-3], history of foot surgery[1] Foot Deformity[4,5]<br>Previous ulceration, Female[2,3]<br>Loss of sensation[4,5] Abnormal ABPI [4,5] | Cross-sectional or retrospective audit data from limited sites |
| **Outcomes / Prognosis** | Limited published data - Recurrence rates are high (47%)[4]<br>70.9% healing, median time to healing of 229.5 days (7.5 months) (comp 30.8 days for non-infected DM)[6] DMARD associated with a reduced median time to healing (190.5 vs 340 days)[6] | Limited prospective follow-up data |
| **Health economics** | No published data | None |
| **Impact** | Negative impact on health-related quality of life | Qualitative small studies |


**1-** Firth et al. 2006. *Annals of the Rheumatic Diseases*, 65 S11:670. 2- Shanmugan et al. 2011 Clin Rheumatol. June ; 30(6): 849–853
**3-** Davys et al. 2006. *Annals of the Rheumatic Diseases*, 65 S11:669. 4- Firth et al. 2008. Arthritis Care & Research, 59 2:200-205.
5-Firth et al 2014. Clin Rheumatol May;33(5):615-21.
6- Kiroskar et al. (2022) Adv Wound Care (New Rochelle). Dec;11(12):650-656




## Diabetes related Foot ulceration

| Factor | Facts & Figures | Level of Evidence |
|---|---|---|
| **Prevalence** | 1.3% to 4.8% in community setting[1,2] | Large population based study, multiple sites |
| **Incidence** | 2% annual incidence [1,3,4] | Large UK, Netherlands, USA community based studies |
| **Predictive factors** | VPT, MF, absent ankle reflex<br>Plantar pressure, joint deformity[5] | Systematic review and meta-analysis |
| **Outcomes / Prognosis** | Healing rates, re-ulceration rates, amputation rates[6] | Large prospective studies in a number of centres |
| **Health economics** | Annual cost of diabetic foot complications estimated to be £580 million[7] Annual direct costs of hospitalisation in Australia were estimated to be US$238 million[8] | Based on hospital episode data, prospective follow up – Direct hospital costs and data linkage |
| **Impact** | Negative impact on health related quality of life[9,10] | Large cross-sectional surveys, multiple sites |


**1-** Abbott et al. 2002. *Diabetic Medicine*, 20:377-84. **2-** Manes et al. 2002. *Wounds*, 14: 11-15. **3-** Muller et al. 2002. *Diabetes Care*, 25: 570-74. **4-** Ramsey et al. 1999. *Diabetes Care*, 22: 382-87. , **5-** Crawford et al. 2007. *Quarterly Journal of Medicine*, 100: 65-86. **6-** Apelvist et al. 1995. *Foot & Ankle Int*, 16: 388-94. **7-** Kerr et al. *Diabet Med* 2014;31:1498–504. 6: 62-73. , **8-** Graves N, Zheng H. *Wound Practice Res* 2014;22:20–33 **9-** Goodridge et al. 2006. *Foot & Ankle Int*, 27. 274-80. **10-** Ribu et al. 2007. Quality of Life Research16: 179-89

# Common sites and presentation of ulceration

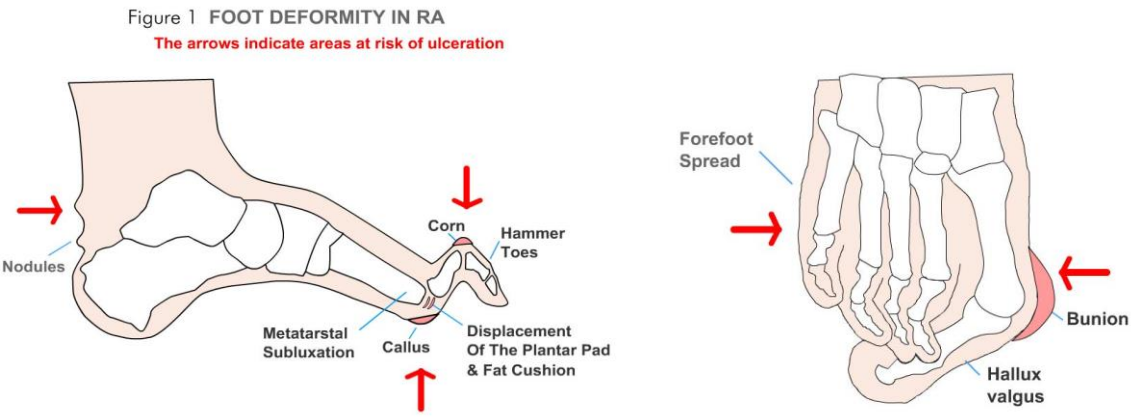



Figure taken from J.Firth / B.Holliday –permission for use granted by the Tissue Viability Society

# Impact of common medications on wound healing

| Medication | Impact on tissue viability |
|---|---|
| NSAIDs<br>(eg naproxen, diclofenac) | Inhibits platelet aggregation and proper coagulation.<br>Risk of haematoma formation (excellent medium for micro-organism growth). |
| Cytotoxic drugs<br>(eg MTX, azathioprine) | May impair wound healing and increase risk of infection. |
| Steroids<br>(eg prednisolone) | Thinned abnormal dermis and epidermis. Interferes with all stages of the wound healing process. Increased risk of infections. |
| Biologic DMARDs Drugs<br>(eg Infliximab, etanercept) | Little is known about the effect on tissue viability and healing.<br>Increased risk of infection. |

# BSR Biologic DMARD safety guideline in inflammatory arthritis (RA, AxSpA, PsA

- Biologics should not be initiated in the presence of serious active infections (defined as requiring intravenous antibiotics or hospitalization; not including tuberculosis) (grade 1B, SOA 98%).
- All biologics should be discontinued in the presence of serious infection but can be recommenced once the infection has resolved (grade 1 A, SOA 99%).
- Use biologics with caution in patients at high infection risk after discussing risks and benefits (grade1B, SOA 99%).
- Consider using Etanercept or Abatacept as a first line biologic therapy in patients at high risk of infection (grade 2B, SOA 94%).
- Health-care professionals should have a high index of suspicion for atypical/opportunistic infections, especially if there is current or recent steroid use. Biologic therapy should be promptly stopped in suspected cases. Patients should have rapid access to specialist health care for consideration of early treatment (grade 1B, SOA 99%)
- Biologic therapies should not be commenced in patients with clinical signs of, or under investigation for, malignancy (basal cell carcinoma excluded) (grade 1C, SOA 96%).
- There is conflicting evidence regarding the risk of skin cancers with anti-TNF therapy; patients should be advised of the need for preventative skin care, skin surveillance and prompt reporting of new persistent skin lesions (grade 1B, SOA 96%).

Strength of recommendation were categorized as either strong (denoted by 1) or weak (denoted by 2), according to the balance between benefits, risks, burden and cost.
Quality of evidence was determined as either high (A), moderate (B) or low/very low (C) reflecting the confidence in the estimates of benefits or harm.
Strength of agreement (SOA) expressed from 0-10 was calculated for each recommendation, by poling all members of the guideline working group. An SOA of 0 denoted complete disagreement and 10 denoted complete agreement.
Recommendations were only included where the mean SOA was $\geq 7$ and $\geq 75\%$ of respondents scored $\geq 7$.

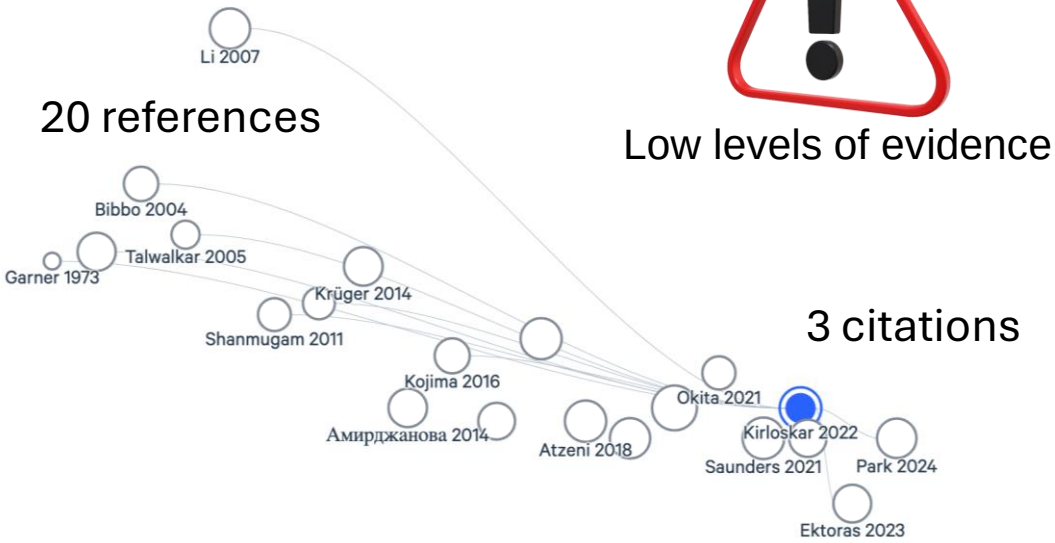
# The Relationship Between Autoimmune Disease and Disease-Modifying Antirheumatic Drugs on Wound Healing

Retrospective review of patients presenting to our wound care center between 2014 and 2018 with both chronic wounds and a history of inflammatory disease. Fifty-eight patients with a total of 296 wounds were retrospectively reviewed.

- Patients were taking at least one DMARD at wound onset in 217 (73.3%) of these wounds
- Only 70.9% wounds progressed to healing compared to healing rates of 97% in patients with noninfected diabetic foot ulcers
- Patients who were taking at least one DMARD at wound onset healed significantly faster than patients who were not on any DMARD therapy at the time of wound onset (190.5 days vs. 340 days, p = 0.016).
- Four patients (5.2%) required major amputation (3 unilateral and 1 bilateral below knee).
- Six patients (10.3%) required minor amputation (hallux, Lisfranc, metatarsal).
- These findings highlight the wound healing challenges posed by underlying autoimmune disease.

Litmaps

Low levels of evidence




**Kirloskar KM, Dekker PK, Kiene J, Zhou S, Bekeny JC, Rogers A, Zolper EG, Fan KL, Evans KK, Benedict CD, Pasieka HB, Attinger CE. The Relationship Between Autoimmune Disease and Disease-Modifying Antirheumatic Drugs on Wound Healing. Adv Wound Care (New Rochelle). 2022 Dec;11(12):650-656.**

# Specific considerations when managing wounds in those with RA

Wounds are often undermined and extremely painful

Pain relief or use of LA can be helpful assist with sharp debridement, consideration of chemical debridement

Drug therapies and autonomic neuropathy may mask the “classic signs of infection”

Can be difficult to decide if there is an infection present or flare in disease status or septic arthritis

Bloods, imaging and swabs may be useful to determine disease activity, presence of an infection or critical colonisation which is delaying healing.

Probing often shows that an apparent superficial wounds tracks down to bone

Consider biopsy for non-responsive wounds (vasculitis / malignancy)

High index of clinical suspicion of osteomyelitis when probe to bone but joint deformities / erosions can make it difficult to assess for the presence of osteomyelitis.

Serial radiographs may need to be undertaken - Think of radiation exposure

# Management challenges

- Wound debridement and dressings often very painful – liaise with rheumatologists and pain clinic for optimum relief.
- Complex foot deformities can make wound dressing very problematic.  Many dressings are too bulky.
- Keeping wound dry can be problematic.
- Many off-loading devices are not suitable for patients with RA (poor balance, falls risk and osteoporosis, weight, fastenings)
- Many patients may have joint replacements making amputation options limited due to infection risk and delayed healing
- Upper limb deformities and loss of strength make rehabilitation challenging
- Consider early  surgical intervention - Osseous integration is a potential future opportunity to minimise higher level amputation

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# Thank you for your attention

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