

Are we Neglecting Rheumatic (iGAS) Diseases in Clinical Practice?

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Abstract

A resurgence of adult cases of invasive group A streptococci (iGAS) in Germany, and other European countries along with UK, the USA, and Canada has been a matter of concern in 2022. Though this resurgence was reported since 2010 of late it is creating sensation in high-income countries (HICs). However, the burden of invasive GAS is less clear in low-income countries (LMICs). The world health organization (WHO) recently reported that *Streptococcus pyogenes* (group A streptococci, or GAS) is a major cause of death and disability globally, particularly in low- and middle-income countries.

The first sign and symptom of infection with invasive group A *Streptococcus* (iGAS) is pharyngitis, mostly in school going aged children. Acute rheumatic fever (ARF) is the result of an autoimmune response to iGAS. A single severe episode or from multiple recurrent episodes of the illness that include sore throat, fever, and fleeting joint pains leading to long-term damage to cardiac valves known as rheumatic heart disease (RHD) or acute post streptococcal infection Glomerulonephritis (APSGN) It is a notable cause of morbidity and mortality in resource-poor settings around the world.

Despite global understanding of disease pathogenesis advancement in recent years, its diagnostic and treatment approaches, are still reliant on clinical features using the Jones Criteria. Penicillin has been the mainstay of treatment for decades and there is no other treatment that has been proven to alter the likelihood or the severity of RHD after an episode of ARF. The use of echocardiographic diagnosis in those with ARF and in screening for early detection of RHD, progress in developing group A streptococcal vaccines and documentation of the life experiences of those with RHD remind the scientific world the need to improve quality of life against this neglected disease affecting worldwide populations particularly those living in poverty.

In India, RHD continues to be a significant cause of cardiovascular morbidity and mortality among children, adolescents, and young adults. This article is to remind medical fraternity and Public Health System that RFD and RHD have not declined, but they have only been neglected in the burgeoning epidemic of lifestyle diseases such as coronary artery disease, diabetes, and hypertension and recent Pandemic of Covid 19 and other communicable diseases.

Materials & Methods:

The current literature and management guidelines are reviewed, with regards to developments from the days of first case of RHD, I saw in 1963 and one case of Rheumatic fever and 2 cases of Poststreptococcal glomerulonephritis in the last 2 years.

Kew Words: archaeological wood; AVS; biological degrada- tion; erosion bacteria; XPS

Introduction

The Robert Koch Institute (RKI) has reported three teenagers with influenza infections died in the German state of Saxony-Anhalt because of secondary infections with invasive group A *Streptococcus* [1]. Despite being in existence for hundreds of years, *Streptococcus pyogenes* (group A streptococci) remains a significant cause of global morbidity and mortality,

with a particular impact in resource-limited settings. Pyogenic β -haemolytic streptococci (including Group A, C and G *Streptococcus*) are some of the most important Gram-positive bacterial pathogens in human medicine. *Streptococcus pyogenes*, (colloquially named “invasive group A streptococcus” (iGAS)), is a pathogen of public health significance, infecting

18.1 million people worldwide and resulting in 500,000 deaths each year. Children, the immunocompromised and the elderly are at the greatest risk of *S. pyogenes* infections and the associated sequelae, with transmission rates being higher in schools, hospitals, kindergartens, and residential care homes [2]. Although effective therapy is available, invasive streptococcal infections are associated with a significant disease burden.

Sixty years ago (1962-63) in our medical college student days, we used to see lots of cases of acute rheumatic fever (ARF), rheumatic heart disease (RHD), a few acute post-streptococcal glomerulonephritis (APSGN), and invasive *S. pyogenes* cases [3]. The world health organization (WHO) had reported that *Streptococcus pyogenes* (group A streptococci, or GAS) is a major cause of death and disability globally, particularly in low- and middle-income countries. The greatest burden is due to rheumatic heart disease which results from damage to heart valves caused by one or several episodes of rheumatic fever, an autoimmune inflammatory reaction to throat infection with GAS. In addition, there is significant burden due to invasive GAS diseases, acute rheumatic fever and post-streptococcal glomerulonephritis, and pharyngitis caused by GAS is a contributor to global antibiotic use. 'Rheumatic Fever and Rheumatic Heart resolution (WHA71.14) has led in 2018 to the development of a Preferred Product Characteristics (PPC) and a R&D Roadmap on GAS vaccines, and guidance to the development of novel GAS vaccines [5].

What was a phenomenon of Low-Income countries (LICs) is increasing in epidemic proportions in some European countries. This rise may be since GAS/iGAS infections only need to be reported in some European countries [4]. The global burden of disease caused by group A streptococcus (GAS) is not known. A 2005 review of population-based data to estimate the burden of GAS diseases highlighted the deficiencies in the available data. The study estimated that there will be at least 517,000 deaths each year due to severe GAS diseases (e.g., acute rheumatic fever, rheumatic heart disease, post-streptococcal glomerulonephritis, and invasive infections). The prevalence of severe GAS disease is at least 18.1 million cases, with 1.78 million new cases each year.

Overall extent of the spread in the European region is not yet clear but typification data indicate that the increase in cases is neither connected to a specific or new strain nor to an increase in antibiotic resistance to GAS. The number of acute respiratory infections (ARIs) in the German population has dropped to 4.7% (Week 1 of 2023). During the previous week, the figure was 7.3%. The Robert Koch Institute (RKI) has inferred that the currently incidence is like that of the pre-pandemic years. The major concern is three teenagers with influenza infections died in the German state of Saxony-Anhalt because of secondary infections.

The incidence of invasive disease caused by group A streptococcus (GAS) has increased in multiple countries in the past 15 years. The burden from infectious disease is high, particularly in low-income and middle-income countries (LMICs). *Streptococcus pyogenes* group A streptococcus [GAS] is an important cause of invasive bacterial disease in the post-partum period and in children. A resurgence of adult cases of invasive GAS in the UK, the USA, and Canada has been reported since 2010. In LMICs, the burden of invasive GAS is less clear than it is in high-income countries (HICs);

Global understanding of disease pathogenesis has advanced in recent years, led to dramatic improvements in diagnostic approaches, that are still reliant on clinical features using the Jones Criteria, or treatment practices. Penicillin has been the mainstay of treatment for decades and there is no other treatment that has been proven to alter the likelihood or the severity of RHD after an episode of ARF. The use of echocardiographic diagnosis in those with ARF and in screening for early detection of RHD, progress in developing group A

streptococcal vaccines and documentation of the life experiences of those with RHD remind the scientific world the need to improve quality of life against this neglected disease affecting worldwide populations particularly those living in poverty [6]. A recent study highlights the gaps in knowledge about the incidence of invasive GAS in LMICs in pregnant women and children and its long-term outcomes [7].

Understanding the epidemiology of invasive GAS is important to design prevention and management strategies like case management and deployment of vaccines.

Case Studies:

1. First ever RHD case seen in my Life:

In my first clinical posting in 1964, in the medical ward, I can across a man of 41 years was admitted with the history of fever, cough and Breathlessness on walking since a week, he also complained of palpitation in the past 3 weeks and cough with sputum over 2 months. The past history revealed multiple episodes of fever and joint pains from the age of 5 years to 15 years, for which he was given Penicillin Injections. There was no other significant information of ill health or surgeries in the past. On physical examination he was afebrile, pulse was 98/minutes and irregular, Respiratory Rate was 18/minutes. On auscultation we could hear mid-diastolic murmur at the apex of the heart without any radiation. This case was the discussion of the day. Bilateral rales were also heard indicating mild bronchial Asthma. Elevated jugular vein distension was also seen. An Xray and CT scan revealed Left ventricular function reduction, The right ventricle was a bit dilated with hypokinetic Right ventricular systolic function, flattened septum consistent with Right ventricular volume overload. There was a severe mitral valve stenosis. The mean and peak gradients were 9 mm Hg and 15mm Hg respectively and the valve area was 1 cm². The case was diagnosed using Jones Criteria.

1. Recent Acute Rheumatic Fever (ARF) case seen:

A 12-year-old girl presented to me with a complaint of pain and swelling in her lower extremities for 3 days, more severe in her left knee over the last 2 days in July 2022. She denied any history of recent or past trauma to that region. She recalled similar previous experiences 6 months ago of pain in right elbow, that subsided with a nonsteroidal anti-inflammatory drug (NSAID). On physical examination, the patient was afebrile with normal blood pressure, pulse rate and respiratory rate. The right lower extremity was normal with no oedema, deformity, or restricted range of motion. On the left side, she showed signs of tenderness in both the medial and lateral aspects of her left knee. She did not have any hepatosplenomegaly, or any other systemic abnormalities. She was prescribed painkillers and sent home. The patient presented again 10 days later with more severe pain in her ankles, wrists, and knees. She reported that the symptoms had not improved since her last visit, and she was unable to come earlier because of her job. There were blanching erythematous plaques over her body, most noticeably over the trunk and back. Subcutaneous nodules were also found on both arms. No murmurs were heard on auscultation and her neurologic examination was without any abnormalities. She was immediately admitted for further examination with a suspected diagnosis of acute rheumatic fever. Lab investigations done included 1) A throat culture was found negative for group A streptococcus, but she had elevated titres of ant streptolysin O (ASO) and ant deoxyribonuclease B (ADN-B). 2) She tested negative for human immunodeficiency virus (HIV), Chlamydia trachomatis, Neisseria gonorrhoeae and syphilis. 3) She had an elevated white blood cell count of 14.6/mm³ with an elevated erythrocyte sedimentation rate (ESR) of 62 mm/h. Her haemoglobin was normal at 12.2 g/dl. 4) Her ECG (electrocardiogram) and echocardiogram (ECHO) revealed no

abnormalities. On treating her with aspirin symptoms gradually subsided over the next 48 hrs. She was discharged on high dose aspirin and oral penicillin and scheduled for regular cardiac follow-ups. At each visit, her WBC count, ESR, bleeding profiles, ASO and ADN-B levels monitored, and a cardiac echocardiogram was performed. She is fine with no cardiac involvement so far.

2. A case of Glomerulonephritis:

Smitha a 15-year-old girl presented to me in November 2022 complaining of swollen hands and feet's for the last week. She had also noticed that over the last two days she noticed swelling around her eyes and was short of breath. No significant history, but both parents suffered from Hypertension and diabetes for over 10 years. She is the youngest of the 5 siblings. *Clinical examination revealed:* an awake and alert, girls with periorbital oedema, bilateral oedema of the hands and feet and mild tachypnoea at rest. Temperature: 37C, afebrile, BP:150/95 mmHg, hypertensive, HR:85 beats per minute, tachycardic and RR:20 breaths per minute, tachypnoea. There was a mild conjunctival and tongue pallor. On auscultation Bilateral basal crackles were heard. Abdomen, CNS and Skin examination did not show any significant signs but there were a few mild scarring from healed lesions noted on thighs may be due to scratching after itching. *Key biomarker changes in* a) blood examination was raised Urea-**28** (2.5-6.4 mmol/L), Creatinine-**650** (50-80 umol/L) and Potassium (K)- **6.1** (3.3-5.0 mmol/L). b) Urine examination- Urine Dipstick test showed i) *Blood*- 4+ and ii) Protein= 2+. C) Xray chest and d) ECG were normal. This case is a typical form of acute & diffuse proliferative glomerulonephritis following an infection caused by group A beta-haemolytic streptococci throat infection. The patient responded well to diuretics and antibiotics over next 10 days. The major effort was to control fluid balance and BP.

3. Poststreptococcal acute glomerulonephritis case report of an elderly male:

A 71-year-old man was admitted to a private hospital in Bengaluru in first week of January 2023, with a complaint of pain and swelling of the right ankle and Knees. He had a history of recurrent arthritis, Hypertension, and diabetes mellitus for nearly 20 years. He used Ibuprofen 400 mg {a non-steroidal anti-inflammatory drug (NSAIDs)}, together with daily glimepiride, metformin, and beta blockers and potassium citrate-sodium citrate hydrate. On admission, his body temperature was 37.1 °C and blood pressure was 140/75 mmHg. Bilateral lower leg oedema and swollen right ankle and knee were observed. He gave history of half a dozen throat infections, fleeting joint pains in childhood. Laboratory tests revealed high levels of white blood cells (14,300/ μ L) and C-reactive protein (15.92 mg/dL), an elevated creatinine level (3.28 mg/dL). On the next day, he complained oliguria, no response to diuretic drugs prescribed and his creatinine increased to 5.81 mg/dL. He was put on haemodialysis for next 3 days. He was put on antibiotics and steroids injection for his joint pain, that promptly improved. NSAIDs-associated nephropathy was suspected, yet his renal function did not show improvement, therefore was put on dialysis. While providing symptomatic treatment, a renal biopsy was done on day 7. That showed 25 glomeruli, including ten global scleroses. IF staining for nephritis-associated plasmin receptor (NAPlr) and in situ zymography for plasmin activity were strongly positive. The final diagnosis was 'PSAGN combined with small vessel vasculitis'. The patient recovered over a period of 3 weeks and is under observation till day.

Discussions:

Acute rheumatic fever has a worldwide incidence of 19 cases per 100 000. The annual incidence varies from 0.5 per 100,000 in the USA, to 8 -51 per 100,000 in children and young adults in developing countries [6]. In India

the prevalence of RHD is estimated at around 0.9 cases per 1000 children in the age-group of 5-14 years. Presuming 20% of the country's total population is in 5-14 years age-group, it is estimated that there are around 2.18 lakh cases of RHD in the country [7]. A 2022 retrospective study of 307 patients out of 402 records screened, included 188 male (61%) and 119 female patients (39%) of mean age 9.73 ± 3.45 years at diagnosis. A family history of acute RF or RHD was documented in 23%. A larger household was significantly associated with an increased incidence rate of acute RF ($P < 0.001$). Nearly two thirds of patients (77%) had multiple joints involved with fleeting characteristics and in only 10% one joint only. The joints involved were in order of highest prevalence were Knees (63%), ankles (57%), small joints of hand & feet (28%0 , Hip (21%), wrist (15%), elbow (12%), spine (7%) and shoulder 965). Carditis was found in (52%); Of them 147 (92%) had mitral valve insufficiency and 109 (68%), Steroid therapy was given to 31 patients with severe carditis and the remaining carditis patients received acetylsalicylic acid. Cardiac failure developed in 21 patients 5 of these patients' required admission to the ICU [9].

The pooled prevalence of GAS pharyngitis among asymptomatic children and pharyngitis cases aged 5 to 15 y was estimated as 2.79 percent and 13 percent respectively. The prevalence rate of rheumatic fever was 0.04%. The pooled prevalence rate of RHD among children aged 5–15 y using clinical auscultation and echocardiography was estimated as 0.36% and 0.28% respectively [9].

Diagnosis of ARF is currently based on the Jones criteria [8]. Five major criteria were carditis, arthritis, chorea, erythema marginatum, and subcutaneous nodules, whereas the minor criteria are arthralgia, hyperpyrexia, high erythrocyte sedimentation rate (ESR), and/or high C-reactive protein (CRP), and prolonged PR interval. For making a diagnosis of acute rheumatic fever, two major, or one major and two minor manifestations must be accompanied by supporting evidence of antecedent group A streptococcal infection in the form of positive throat culture or elevated or rising anti-streptolysin titre. The revised criteria as of 2015 suggests Major criteria: carditis (clinical and/or subclinical), polyarthritis, chorea, Erythema marginatum, and subcutaneous nodules. Minor criteria: Polyarthralgia, fever ($\geq 38.5^\circ$ F), sedimentation rate ≥ 60 mm and/or C-reactive protein (CRP) ≥ 3.0 mg/dl, and prolonged PR interval. The last revision of the Jones criteria consists mainly in the supplementation of the major criteria with echocardiographic examination, the introduction of a concept of subclinical carditis and the isolation of low, medium and high-risk populations among the patients [8].

Current Recommendations for RHF management:

i. Prevention of rheumatic fever in patients with group A beta haemolytic streptococci (GABHS) pharyngitis-Oral (PO) penicillin V remains the drug of choice for treatment of GABHS pharyngitis, but ampicillin and amoxicillin are equally effective. When PO penicillin is not feasible or dependable, a single dose of intramuscular benzathine penicillin G, or benzathine/procaine penicillin combination is advised. For patients allergic to penicillin, alternate administration of erythromycin or a first-generation cephalosporin or clarithromycin for 10 days, or azithromycin for 5 days are recommended. Tetracyclines and sulphonamides to treat GABHS pharyngitis are not advocated. **For recurrent group A streptococci (GAS) pharyngitis**, a second 10-day course of the same antibiotic may be repeated. *Exposed persons:* People in contact with patients having documented cases of streptococcal infection first should undergo appropriate laboratory testing if they have clinical evidence of GABHS infection and should undergo antibiotic therapy if infected. *School and childcare centres:* Children with GABHS infection should not attend school or childcare centres for the first 24 hours after initiating antimicrobial therapy [11, 12]

Mnemonic: "JONES CAFE PAL"

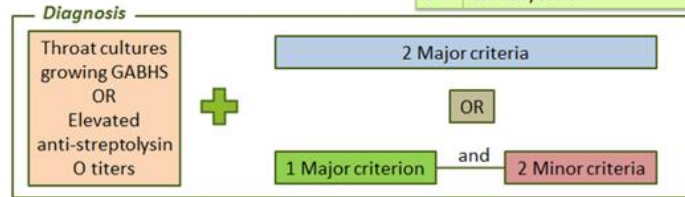
Major Criteria

J	Joint Involvement
O	O looks like a heart = myocarditis
N	Nodules, subcutaneous
E	Erythema marginatum
S	Sydenham chorea

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Minor Criteria

C	CRP Increased
A	Arthralgia
F	Fever
E	Elevated ESR
P	Prolonged PR Interval
A	Anamnesis of Rheumatism
L	Leukocytosis



GABHS carriage status is difficult to eradicate with conventional penicillin therapy, therefore PO clindamycin (20 mg/kg/d PO in 3 divided doses for 10 days) is recommended. Antimicrobial therapy is not indicated for pharyngeal carriers of GABHS except during outbreaks of rheumatic fever or poststreptococcal glomerulonephritis, Family history of rheumatic fever, during outbreaks of GAS pharyngitis in a closed community and when tonsillectomy is considered for chronic GABHS carriage [11]

ii. Treatment for patients with rheumatic fever

Therapy is directed towards eliminating the GABHS pharyngitis (if still present), suppressing inflammation from the autoimmune response, and providing supportive treatment of congestive heart failure (CHF). Residual GABHS pharyngitis, if still present as also treated similarly. Treatment of the acute inflammatory manifestations consists of salicylates and steroids. Aspirin in anti-inflammatory doses effectively reduces all manifestations of the disease except chorea, and the response typically is dramatic. If rapid improvement is not observed after 24-36 hours of therapy, reconsider the diagnosis of rheumatic fever. When discontinuing therapy, aspirin is to be withdrawn gradually over weeks while monitoring the APRs for evidence of rebound. Chorea most frequently is self-limited but may be alleviated or partially controlled with phenobarbital or diazepam [12].

If moderate to severe carditis is present as indicated by cardiomegaly, third-degree heart block, or CHF, adding oral prednisone to salicylate therapy is recommended. Prednisone needs to be continued for 2-6 weeks based on the severity of the carditis and tapered during the last week of therapy. Maintaining salicylates for an additional 2-4 weeks, can minimize adverse effects. Include digoxin (after checking serum Potassium) and diuretics, afterload reduction, supplemental oxygen, bed rest, and sodium and fluid restriction as additional treatment for patients with acute rheumatic fever and CHF. The diuretics most used in conjunction with digoxin for children with CHF include furosemide and spironolactone. The total loading dose is 20-30 mcg/kg PO every day, with 50% of the dose administered initially, followed by 25% of the dose 8 hours and 16 hours after the initial dose. Maintenance doses typically are 8-10 mcg/kg/d PO in 2 divided doses. For older children and adults, the total loading dose is 1.25-1.5 mg PO, and the maintenance dose is 0.25-0.5 mg PO every day. Therapeutic digoxin levels are present at trough levels of 1.5-2 ng/mL. Afterload reduction (ie, using ACE inhibitor captopril) may be effective in improving cardiac output, particularly in the presence of mitral and aortic insufficiency. Start these agents judiciously.

Use a small, initial test dose and administer only after correcting hypovolemia [11,12].

Treatment for patients following rheumatic heart disease (RHD)

Preventive and prophylactic therapy is indicated after rheumatic fever and RHD to prevent further damage to valves. Primary prophylaxis (initial course of antibiotics administered to eradicate the streptococcal infection) also serves as the first course of secondary prophylaxis (prevention of recurrent rheumatic fever and RHD). An injection of 0.6-1.2 million units of benzathine penicillin G intramuscularly every 4 weeks is the recommended regimen for secondary prophylaxis for most patients. Administer the same dosage every 3 weeks in areas where rheumatic fever is endemic, in patients with residual carditis, and in high-risk patients. Patients with rheumatic fever with carditis but no valve disease should receive prophylactic antibiotics for 10 years or well into adulthood, whichever is longer. Finally, patients with rheumatic fever with carditis and valve disease should receive antibiotics at least 10 years or until aged 40 years [12].

Presentation and Treatment for Post Streptococcal infection Glomerulonephritis (PSGN):

The most common presenting symptom is gross haematuria as it occurs in 30 to 50% of cases with acute PSGN; patients often describe their urine as rusty. The haematuria is usually a post-pharyngitis phenomenon. Renal involvement is common and is transient with recovery in 1-2 weeks. Less than half of the patients experience oliguria. Depending on the severity of renal involvement, signs, and symptoms suggestive of anuric renal failure or life-threatening acid-base imbalance, hyperkalaemia, and fluid overload would require RRT. About 60-80% of the patients experience high blood pressure which typically resolves in 10 days as was in our case. The incidence of oedema is seen in about 65-90% of the cases. Periorbital oedema is typical for the nephritic syndrome [13]. It is most prominent in the morning and tends to resolve at the end of the day. Generalized oedema is also a common feature. Some patients might experience respiratory distress because of pulmonary oedema. Some may experience anorexia, malaise, nausea, vomiting, etc [8]. Poststreptococcal acute glomerulonephritis (PSAGN) in the elderly tends to have a severe clinical course and often presents with crescentic necrotizing glomerulonephritis in the renal biopsy [14].

Conclusion:

- The exact burden of RFD and RHD is not available and is almost impossible to estimate because of the multiple shortcomings with the available data.
- Indian study emphasizes the importance of developing a population-based surveillance framework to track patterns, management strategies, and outcomes to develop informed recommendations for launching contextual measures to regulate RF and RHD.
- The development of a successful anti-GAS vaccine remains outstanding, due to the inherent challenges, and lack of urgency in Government of India that did wonders in Covid 19 vaccine.
- Emphasis must be placed on creating awareness among the community about the fact that sore throat in their child may not be as benign, and about its serious repercussions, if left untreated.
- The surveillance of pharyngitis among school-aged children and the knowledge about differentiating viral and bacterial pharyngitis and the importance of early diagnosis and treatment of streptococcal pharyngitis must be widely disseminated among primary care physicians. However, the prevalence of GAS among asymptomatic children is a twist to this tale.

References:

1. (2023). Three Teenagers with Influenza Die After Secondary Infection, Michael van den Heuvel
2. Nelly Janira Avire, Review of Streptococcus pyogenes: Public Health Risk Factors, Prevention and Control.
3. Amy Sims Sanyahumbi et. al, (2016). Global Disease Burden of Group A Streptococcus.
4. Beta-Haemolytic Group A, C and G Streptococcal Infections in Southern Hungary: A 10-Year Population-Based Retrospective Survey (2008–2017) and a Review of the Literature, A Mária Gajdács,
5. Immunization-vaccines-and-biologicals/-streptococcus-pyogenes,
6. Jonathan R. Carapetis et.al, Nat Rev Dis Primers 2, 15084 (2016). Acute rheumatic fever and rheumatic heart disease.
7. Emma Sherwood et.al, Invasive group A streptococcal disease in pregnant women and young children: a systematic review and meta-analysis.
8. A Saxena, Indian J Pediatr. (2000). Diagnosis of rheumatic fever, Jones Criteria, and role of echocardiography, 67(4):283-286.
9. Jyoti Dixit et.al, (2022). Burden of Group A Streptococcal Pharyngitis, Rheumatic Fever, and Rheumatic Heart Disease in India: A Systematic Review and Meta-Analysis, Indian Journal of Paediatrics volume 89, pages642–650.
10. Balaji Arvind & Anita Saxena, (2022), Rheumatic Heart Disease in India: Has It Declined or been Forgotten? Indian Journal of Paediatrics volume 89, pages637–638.
11. Rotem Tal et.al, 20 (2022). Rheumatic fever in a developed country – is it still relevant? Pediatric Rheumatology volume 20.
12. Handbook on Prevention and Control of Rheumatic Fever and ... > sites > default > files
13. A-case-of-swollen-hands and feet's,
14. Keiko Yano, et.al, Crescentic poststreptococcal acute glomerulonephritis accompanied in an elderly male, /10.1186/s12882-019-1663-1669.



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