API DK LAHARI

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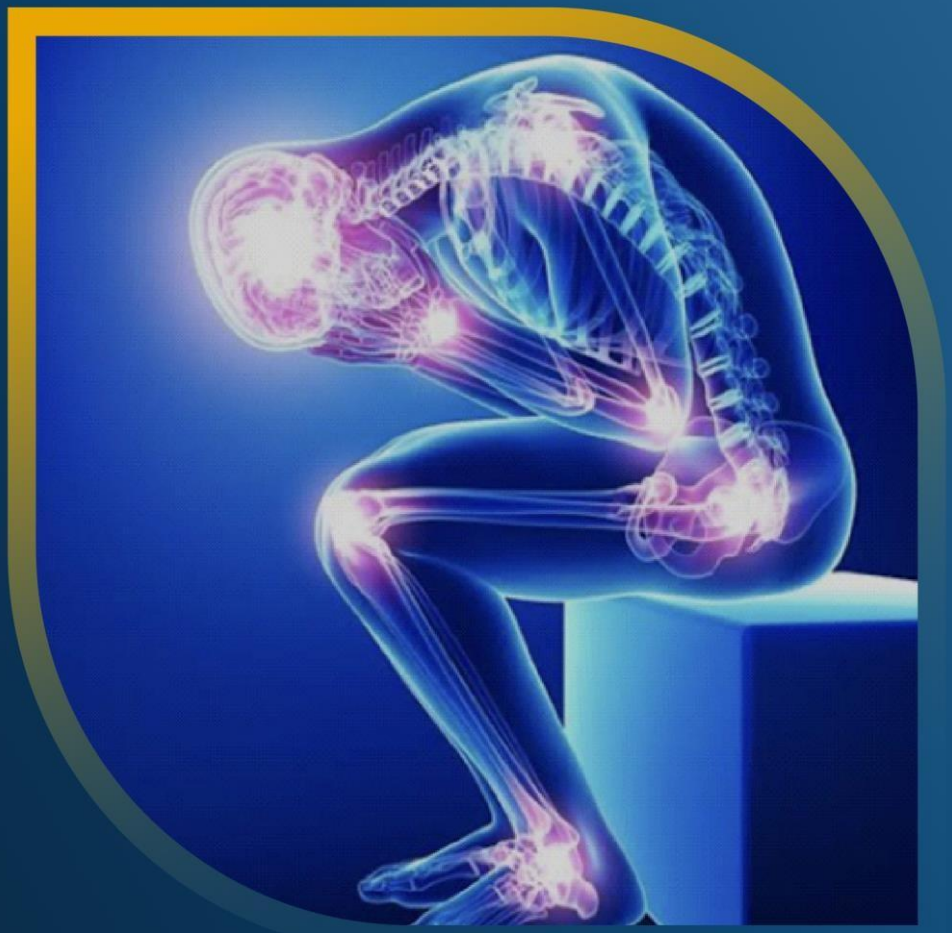

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Guest Editor

RHEUMATOLOGY FOR PHYSICIANS

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PRESIDENT'S MESSAGE

President`s Desk

DR.PRABHA ADHIKARI

Esteemed API Members

It was a pleasure being the President of this Prestigious API DK chapter .We took over last year with great enthusiasm and scientific temperament. I am very glad that we were able to hold 12 Meeting cum CMES and one online CME. We were able to hold MAPICON 2023 with great participation from members and Postgraduates. National conference of Geriatric Society of India was also organized with the support of the office bearers and members of API D.K.Chapter and Karnataka.

I thank all the members who attended the meetings especially senior members who made it despite the odd timings of the meetings. I could not attract many lady members and all the senior members due to the time of the meeting and length of the meeting .Many of the members have suggested that meeting should be limited to only one speaker .We could not honour their request due to obvious reasons .May be the next team will implement it

To get more members ,atleast one meeting in a year should be planned between 7 PM-8PM or during day time on a holiday or Sunday .Annual family picnic is one way to get to know the family members of our own members .We were happy to find some of the talented family members on the talent `s day .Picnic in a nearby resort with family would give our extremely hardworking physicians a break from the routine .

I am glad our members made it to National APICON CME as faculty this year thanks to our connection with API Karnataka Chapter. More DK chapter members should become API Karnataka chapter members so that they are eligible to become office bearers at State and National level .

I congratulate the editorial team for bringing out this issue of API-LAHARI with Rheumatology as its theme on time .We have missed release of one issue which was purely due to our ignorance that API office bearers are responsible for the logistics of bringing out an issue.

As this is the month of the woman`s day, I wish all the lady members a happy woman`s day a happy month and a happy year and request all to join us for the meeting of the month.

With warm regards

DR.PRABHA ADHIKARI

President

API DK CHAPTER

PROFESSOR AND HOD

DEPARTMENT OF GERIATRIC MEDICINE

YENEPOYA MEDICAL COLLEGE, DERALAKATTE, MANGALORE

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VOICE OF EDITORS

THE EDITORIAL TEAM

Dear colleagues,

We are happy to present the 12th issue of API-DK LAHARI. The theme of this issue is Rheumatology for Physicians. The editorial board is grateful to the guest editor Dr Gangarathna Krishna, Consultant Rheumatologist for overseeing this academic feast with a myriad of articles on various aspects of rheumatology and you will agree that the issue has successful in showcasing the beauty and diversity of rheumatology. In addition to the articles related to the theme, the issue also has nonacademic article by Dr Joe Verghese, legal article by Dr Sadananda Naik and many more. This happens to be the last issue of Lahari under the present editorial board and we are thankful to the API-DK presidents of last two years who supported us in all possible ways. We request you to continue the same kind of support to the new editorial team headed by Dr Archith Boloor and Dr Archana Bhat and hope that our E-Magazine API-DK LAHARI touches greater heights in the years to come.

DR B.SADANANDA NAIK

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API DK CHAPTER SECRETARY'S REPORT

DR.HAROON H

SECRETARY, API DK CHAPTER

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KMC HOSPITAL, MANGALORE

Good day, esteemed members! Before delving into the report, I'd like to extend a warm and respectful greeting to each one of you. I hope this message finds you in good health and high spirits. First off, let's proceed with the details of the report at hand. During the period from December 2023 to February 2024, the API DK Chapter has been active in fulfilling its responsibilities and objectives.

The API DK Chapter has been active and productive during the period from December 2023 to February 2024.Several key activities and accomplishments took place during this time frame.

The MAPICON 2023 conference in Mangalore was a comprehensive event that delved into various aspects of medical practice and research. The inclusion of multiple orations, workshops, and case discussions provided a rich platform for learning and knowledge exchange.

Inaugurated by Dr. B.H. Krishnamoorthy Rao and Dr. Ramesh Pai, the conference commenced with a ceremonious opening ceremony, attended by prominent guests and esteemed delegates from several medical institutions. The conference had a total of 200

registered attendees and 25 faculty members, making it a successful gathering of medical professionals.

The Dr.K.P. Ganesan Memorial Oration on "Preoperative Cardiac Evaluation for Non-Cardiac Surgery" by Dr.R.L.Kamath and the Dr.V.V.Mody Memorial Oration presented by Dr.Venkatesh B.M. served as thought-provoking sessions, shedding light on critical medical topics. Additionally, the lecture on "Optimizing Stroke Prevention in AF Management: Translating Evidence into Clinical Practice" by Dr. Maneesh Rai provided valuable insights for practical application in the field.

The case discussions added another layer of depth to the conference, addressing neurological, gastroenterological, haematological, pulmonary, and rheumatological issues. The involvement of experts from renowned medical institutions enriched the discussions and offered diverse perspectives on managing complex cases.

The experts discussed various cases, including a neurology case by Dr. Alaka Ganesh from GKNM Hospital in Coimbatore, Dr. Balakrishna Valliot from Kannur Medical College, and Dr. Salma Suhana, an Associate Professor of Neurology at Yenepoya Medical College. Additionally, the group examined a gastro case with insights providedby Dr. Anita Basavaraj and Dr. Veena Pinto; a haematology case led by Dr.Rajesh Krishna, Professor of Hametooncology at YMC; a pulmonology case moderated by Dr.Rajesh , Professor of Pulmonology at YMC; and finally a rheumatology case was discussed through the expertise of Dr.Prakruthi Subodh and Dr.Pratibha Pereiera.

Furthermore, the presentation of 40 General Medicine papers and posters showcased the latest research and findings in the field. The recognition of the top papers and posters with cash prizes not only encouraged scholarly contributions but also highlighted the commitment to advancing medical knowledge. The overwhelmingly positive feedback from attendees, emphasizing the practical relevance of the sessions, stands as a testament to the impactful nature of MAPICON 2023. The active engagement and participation of esteemed faculty members and medical professionals further elevated the quality of the conference, making it a valuable platform for learning and networking.

The MAPICON 2023 conference in Mangalore served as a pivotal event for the medical community, offering a comprehensive platform for knowledge exchange and learning. The

inclusion of diverse orations, workshops, and case discussions facilitated a multifaceted exploration of critical medical topics, enriching the experience for attendees.

PHYSICIANS AND FAMILY DAY JANUARY 2024

The Dakshina Kannada Chapter of the Association of Physicians of India (API) organized the Physicians Day event along with Family Day at the IMA Hall in Mangalore on Friday 19th of January 2024.

In memory of the late Professor KR Shetty, former Principal and Neurology professor at Kasturba Medical College, Mangaluru. Dr. MV Prabhu from Kanachur Medical College offered condolences forProf. Shetty, emphasizing his humility and influence on shaping modern KMC.

Dr.IG Bhat, a senior neurologist, commended Prof. Shetty's dedication to truth and ethics while Dr. Joe Varghese discussed his contributions to the medical field and humanitarian endeavors.Dr.BHK Rao also recounted personal experiences from his time working with Prof.Shetty. The event began with a tribute to the role of physicians in providing healthcare services. The importance of physicians innthe healthcare system was highlighted during the event.

The event was a deeply touching and poignant commemoration of the late Professor KR Shetty, with heartfelt speeches and personal anecdotes shared by his students and peers. The presence of esteemed senior physicians and the recognition of their tireless dedication to the medical field added a sense of reverence and solemnity to the occasion.

In addition to honouring the past, the event also served as a platform to acknowledge the invaluable contributions of the present generation of physicians. The felicitation of Senior Physicians Dr. Devdas Rai, Dr. Harold Mascarenhas, and Dr. EVS Maben underscored the significance of their on-going commitment to the well-being of the community.

The program featured fun games, and an entertainment segment, and dinner for the guests, creating a memorable and respectful gathering in honor of Physicians Day and to pay tribute to the late Professor KR Shetty.

As the evening progressed, the atmosphere transformed into one of camaraderie and celebration, as physicians and their families came together to enjoy the entertainment and

engage in lighthearted activities. The lively energy in the air spoke volumes about the strong bond and unity among the medical community in Dakshina Kannada.

Under the leadership of Dr. Prabha Adhikari , the event encapsulated the spirit of gratitude, camaraderie, and professional excellence. It was a fitting tribute to Physicians Day and a heartfelt remembrance of the late Professor KR Shetty, leaving a lasting impact on all those in attendance.

FEBRUARY 2024

The February meeting was truly eventful and productive, setting the stage for a year filled with impactful initiatives and The monthly gathering of the Association of Physicians of India, Dakshina Kannada Chapter, took place at the Hotel Ocean Pearl in Mangalore. It was a significant day on Friday, February 16th, 2024 as members engaged in enriching activities including the Continuing Medical Education session for professional development, an insightful general body meeting to discuss important matters, and a productive magazine committee meeting aimed at enhancing communication within the medical community.

The general body meeting was marked by a high level of engagement from members, with lively discussions leading to important decisions about upcoming events and new initiatives. Key topics centered on the selection of the new team of office bearers for the upcoming year and delving into potential collaborations with healthcare institutions in the region. The conclusion of the meeting left an impression of enthusiasm and determination among members, as they collectively pledged to collaborate towards advancing healthcare in the community and propelling the organization to greater success.

The CME Program:

Panel Discussion on Management of Diabetic Foot and Peripheral Vascular Disease

Moderator:

Dr. Shrinath Prathap Shetty, Endocrinology Consultant

Panelists:

- Dr. Praveen Chandra Nayak, Podiatric Surgery Consultant
- Dr. Priyatham Kamath, Podiatric Surgery Consultant

- Dr. Iresh Shetty, Cardiothoracic and Vascular Surgery Consultant
- Dr. Gautam Shetty, Plastic Reconstructive Microvascular & Cosmetic Surgery Consultant
- Dr. Thomas Joe, Plastic and Cosmetic Surgery Consultant

The CME program delved deep into the latest advancements in Diabetic Foot and Peripheral Vascular Disease management, offering a comprehensive exploration of these critical areas. Post-event, an insightful and dynamic discussion ensued, complemented by a well-attended dinner gathering with 45 participants.

The evening concluded with key takeaways from the discussions that provided valuable insights for all attendees. During the general body meeting, several important matters were discussed and decisions were made

The CME Program and general body meeting, along with the magazine committee session, demonstrated a high level of productivity, emphasizing a shared dedication to improving communication within the medical field collaborations to further the goals of the API DK Chapter.

In conclusion, the efforts and dedication shown by the members of the Association of Physicians of India, Dakshina Kannada Chapter, have been truly commendable. The collaborative spirit, active participation, and commitment to continuous medical education and community well-being are the cornerstones of our chapter. We shall strive to maintain this momentum and keep building on our achievements. Looking forward, it's essential that we continue to engage in innovative initiatives, foster a supportive environment for professional growth, and uphold our commitment to healthcare excellence.

Here's to a future of shared successes and impactful contributions to the medical field.

Long live API

DISCLAIMER

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RHEUMATOLOGY GUEST EDITORIAL

Dr GANGARATHNA KRISHNA

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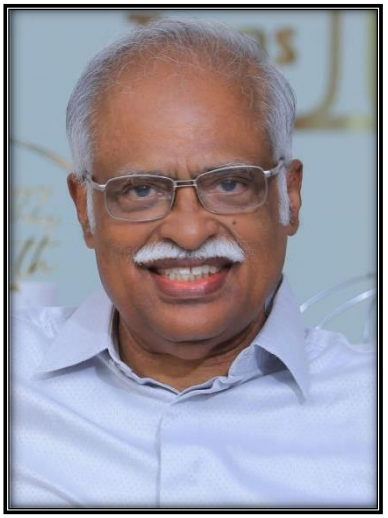
Rheumatic or musculoskeletal conditions comprise over 150 diseases and syndromes, which are usually chronic, progressive, and associated with pain and disability leading to loss of work, income and regular expenditures on treatment. Rheumatological conditions include immune-mediated inflammatory arthritis and connective tissue diseases, degenerative, infectious and metabolic causes of arthritis, regional musculoskeletal disorders, and musculoskeletal pain.

For many years, oral treatments with steroids were the mainstay of management along with disease modifying agents like methotrexate and antimalarials . Now for several rheumatic diseases there is treat to target (T2T) initiative where both outcome and treatment goals have been defined. Treatments with biologics and smaller molecules have revolutionized the management .Doctors caring for rheumatology patients with active disease should refer the patients to rheumatologists at the earliest to optimize their treatment and prevent disability.

The demand for rheumatology care is consistently exceeding the workforce worldwide. This negatively impacts the care of patients with rheumatic and musculoskeletal diseases. There is growing need for trained rheumatologists and training in rheumatology should commence right from undergraduate period. We have Indian Rheumatology Association which is doing tremendous work in increasing the awareness of rheumatological conditions in public, patients and increasing training opportunities for our physicians both in India and abroad. We ,the rheumatologists of Mangalore are wholeheartedly doing our bits in this regard . I am extremely thankful for API DK chapter for including rheumatology theme in this edition of Lahari and giving us the opportunity to showcase the beauty and diversity of rheumatology.

PHYSICIAN & SPECIALIST; A SECOND OPINION



Dr. JOE VERGHESE M.D.

PROF. OF MEDICINE (RETD.) KMC, MANGALORE.

FOUNDER- DIRECTOR,

OMEGA HOSPITAL, MANGALORE.

Driving from Mangalore to Kochi, many years ago in my then gleaming new Ambassador car, I was forced to turn into a small village garage on the highway. 'My problem from the beginning was that after driving continuously for about 100 kms. the car would for no reason slow down. Since my car was still in the warranty period, I had shown my car to the Sales & Service centre which was right opposite my consultation chamber. Since most of the employees there were my patients, they took good care. The electrical specialist suspected engine arrhythmia and cleaned the points and changed spark plugs, the fuel injection expert performed a plasty on clogged fuel pipes, gear box specialist tackled transmission defects and so on and so forth. At the end of it they gave me a detailed discharge sheet of work done and parts replaced with copy to the manufacturer for possible reimbursement. My problem remained. In the wayside garage was this guy in a lungi, patently a general practitioner, who carefully heard me out and took the car for a spin with me sitting by his side. During a 1 km. drive he accelerated quickly, braked violently, drove zig zag and also with the ignition off and the gear in neutral. We came back to the garage and he barked a short order in Malayalam to his assistant to emove the left rear wheel and adjust the brakes. Within 30 minutes the job was over. While paying up his bill of Rs. 150/- I asked him what

was wrong. Being a man of few words, he told me that the brake unit during long running was heating up and jamming. All he did was some readjustment and I never had that problem for the few years I used the car. 1 Today many patients are in a similar plight. The diseased body has been divided and now is the sum total of the various systems and organs, which are handled by different specialists at various times. No one person can be blamed for this very much prevalent practice, but everyone of us doctors and often patients have contributed knowingly or unknowingly to the genesis and propagation of this serious anomaly. The Physician is often referred to as a Jack of all trades and Master of None. In contrast a super specialist is mischievously described as one who learns more and more about less and less and ultimately and logically ends up by knowing everything about nothing. As long as both General Physician and Specialist work closely and in tandem the common mistakes, of omission and commission in patient management can be avoided. Every successful and effective set up has a foreman, a coordinator, a captain or a leader. Whether it be a rocket launch programme, a big ocean liner, a huge building under construction, a football team or for that matter cabinet ministers, all the individual experts work in unison under one person who is with them and is a part of them. An orchestra plays under the baton of the conductor. Though the conductor himself may not be proficient in any musical instrument, he still controls the tune and timing of the many instruments, the pitch and voice of the choir, all of which is blended beautifully into a soul stirring melody. This should be the philosophy when a complex problem, involving multiple organs and systems in a patient is being addressed. The physician having assessed the patient should call in the required specialists for specific purposes of procedures, management etc. Multiple specialists may be needed at different times or together, but the team leader should ensure that the protocols are complimentary without adverse interactions or avoidable contradictions. This is a win-win situation for all concerned and the ultimate beneficiary is the patient who had the best of everything and everybody. It is unfortunate that for a variety of reasons the patient's do not get need based care. Our late revered Professor, Dr. K. P. Ganesan used to often tell his students that the only person who is truly a general physician is the clerk sitting in the 'OP counter of the General Hospital asking the patient the nature of his complaints and then making an OP ticket directing him to the proper department. Though this is the essence of the matter before us, yet unfortunately many extraneous factors operate. Sometimes it is the physician who has a feeling of

knowing it all, the specialist who has a little contempt for the generalist and to top it all the patient after making a Google diagnosis on himself, decides whom to consult. Very surprisingly we often have patients who are being treated simultaneously and separately by a cardiologist, an endocrinologist etc., and sometimes when nothing works by a physician. By definition and practice a specialist though excelling in his own field, has a restricted vision and a biased thought process. I am sure many of us in Mangalore remember the sad case of a young doctor practicing a super speciality in surgery. This doctor developed severe burning sensation in his chest. He thoughtfully considered all possibilities that struck him and underwent an upper Gl endoscopy, an abdominal scanning to rule out other upper abdominal pathology over the course of 2 days. Tragically he collapsed and died at work, the victim of a massive myocardial infarction which was not considered at all, partly due to the mistake of treating himself and more importantly having that lack of perception which is directly attributable to his specialized training and exclusive practice resulting in missing the common and the obvious for something familiar and usual to him. : Between the zealous doctor and the erring patient is another smart aleck who has recently emerged and is now presiding over the destinies of both. He is a management expert who calls the shots in the large corporate hospitals. He neither realizes nor respects the fragile but sacred bond between the doctor and patient. He justifies his means towards the end of increasing the revenue of the Hospital, which he achieves by dangling a carrot before the doctor and a scarecrow before the patients. The challenge in medicine is in the clinical diagnosis, whereas the money is * in the machine diagnosis. As a consequence we find that in a big setup, the name of physicians is a formality or only an appendage in the list of in-house doctors. They are usually relegated to the task of conducting complete medical check up', which perhaps is often of doubtful value to the patient, but very valuable to the hospital. (In many developed western countries the general practitioner sees the patient first and then decides about reference to a higher centre or specialist. In a backward rural setup there is only a GP available. It is unfortunate that it is only in the semi urbanized, semi-knowledgeable but affluent societies that GP and Physicians are discounted and specialists are forced, much against their wishes to be the first line of defence which is neither necessary nor appropriate. All said and done the sad fact is that as of now the role of the general physician is mutating to possible eventual extinction. It has been partly abdicated and partly annexed. Let us not forget the immutable fact that a person has body, mind and a spirit, all of which

are always effected together, perhaps unequally, by any disease process. The three cannot be separated nor can any single one of them be divided.

One could daresay that there may not be a’ single disease entity that effects just one organ or system. Only a physician will have the overview, insight and know-how to treat the patient 'whole' & 'soul. The Holy Bible while referring to this truth, records thus "If one part suffers, every part suffers with it; if one part is honoured, every part rejoices with it" (1 Corinthians, 12:26). What God has put together, let no 'man separate. It will be disastrous. In hopeful conclusion of all things, let us wait patiently for the wheel to fully turn, wisdom to dawn even if late and values to be reset. If and then, will the Physician regain his rightful place in the comity of doctors, the management of patients and the well-being of the community. If so, each will work within his assigned role, fight shoulder to shoulder against the common enemy of disease and distress and on being successful as worthy instruments, give credit, never to themselves, but to God Almighty, the true and only Healer.

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No respite for Doctors in the New Criminal Law

Bharathiya Nyaya Samhita Act 2023 [BNS]is all set to replace the existing Criminal Law, Indian Penal Code,1860 [IPC] and would come to effect from1st of July 2024 as per the Government of India Notification. There was a hype in the media that doctors would be out of purview of criminal prosecution once this Law come into force. This short write-up would give an insight into this wide published myth as well as euphoria amongst the medical fraternity in India.

Section 106 of Bharathiya Nyaya Samhita Act 2023 [BNS] equivalent of Section 304A of Indian Penal Code, 1860 [IPC] reads as 'causing death by negligence' and imposes a punishment up to five years along with a compulsory fine which is an enhanced punishment from the two year imprisonment of the IPC, which did not include a mandatory fine.

Part of the Statute reproduced as below

Causing death by negligence 106. (1) Whoever causes death of any person by doing any rash or negligent act not amounting to culpable homicide, shall be punished with imprisonment of either description for a term which may extend to five years, and shall also be liable to fine; and if such

act is done by a registered medical practitioner while performing medical procedure, he shall be punished with imprisonment of either description for a term which may extend to two years, and shall also be liable to fine.

Explanation. — For the purposes of this sub-section, "registered medical practitioner" means a medical practitioner who possesses any medical qualification recognized under the National Medical Commission Act, 2019 and whose name has been entered in the National Medical Register or a State Medical Register under that Act.

As we read the section applicable to us , we could find that the doctors have not been given exemption from the criminal liability but when compared to the general public the quantum of the punishment has been little lesser. However, the guilty doctors are now liable to pay a fine which was not there in the IPC. The special provision of reduced quantum of imprisonment is only applicable to the Registered Medical Practitioners who have enrolled as per NMC Act 2019 and not for any other medical professionals, as of now.

The law is not clear once again about what a rash or negligent act is, when it comes to medical procedure and the courts have to rely upon the judgment of the Supreme Court of India in **Jacob Mathew v State of Punjab 2005** which opined that in order to qualify as rash and negligent act the alleged doctor's act of negligence has to be 'Gross' or 'of very high degree'

EVALUATION AND MANAGEMENT OF TAKAYASU ARTERITIS

DR PRATHYUSHA MANIKUPPAM, DR SHIVRAJ PADIYAR

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INTRODUCTION

Takayasu Arteritis (TA) is a rare form of chronic granulomatous large vessel vasculitis that is more common in Asia compared to other parts of the world. However the frequency is increasing in other parts of the world, partly due to high immigration rates (1). The Annual incidence rate ranges from 0.4–3.4 per million individuals and the prevalence differs from region to region with Japan having the highest prevalence at 40 per million to 9.0 per million in USA (2). TA commonly presents in second to third decade of life, with a female predominance. Disease may have its onset in childhood and children with TA have significant differences in their clinical presentations from adults. Recent studies from Japan and Korea identified differing patterns of arterial involvement in females and males; they found females to have more frequent involvement of thoracic aorta and its branches whereas males were more likely to have abdominal aorta involvement (3,4).

EVALUATION

Based on the clinical suspicion of TA, further tests need to be done to confirm the diagnosis. Various imaging modalities like CT angiography, MR angiography and PET CT is used in the diagnosis and monitoring of TA. CT angiography is the most commonly used modality, mainly for its excellent vessel delineation capacity. However, it comes with its inherent risks of radiation, especially in long term follow up of the disease. The advent of MR angiography has remarkable removed the risk of radiation, but with its drawback like lack of expertise in reporting, availability and cost. Additionally, in the presence of the pre-existent stents, MRI may give an artefact in that area and may prevent the appropriate detection of pathology. PET CT on the other hand allows an earlier detection of TA. Its use in monitoring of the disease is controversial as some uptake may still persist even if the disease is in remission. If the patient has cost constraints or any contraindications for imaging, doppler ultrasonography may give necessary information in the relevant arteries. Doppler of the carotids may demonstrate the typical macaroni sign, which is the smooth homogenous, circumferential thickening of the arterial wall of the carotids. A renal artery doppler needs to be performed in cases presenting with hypertension to rule out the possibility of renal artery stenosis. Laboratory investigations like CRP and ESR are used to assess the disease activity and should not be used for diagnosis of TA. Around 30 percent of TA patients can have normal ESR and CRP at presentation. In order to counter these fallacies, there are various disease activity scoring system in TA. One of the most commonly used is ITAS 2010 (Indian Takayasu arteritis score). The other disease activity scoring systems are NIH (National institute of health) criteria, DEI TAK (Disease extent index in Takayasu arteritis) and TADAI (Takayasu arteritis integrated disease activity index).

TREATMENT

As in any other form of systemic vasculitis, glucocorticoids (GC) form the mainstay for induction of TA. Even though traditionally 1 mg /kg of steroids is used, recent literature suggests that an initial daily GC dose of 0.5 mg/kg/day prednisolone along with upfront steroid sparing agents may be associated with similar rates of early response without increasing the risk of relapse in the longer term. Patients receiving long-term GC should be given due consideration for the prevention of osteoporosis, diabetes mellitus and cataract.

Steroids should always be accompanied by steroid sparing agent either conventional synthetic dmards or biological dmards (5).

CONVENTIONAL DMARDS

The evidence of conventional DMARDs (csDMARDs) in TA is sparse. The only RCT available in this regard, which compared the clinical and angiographic outcomes between Mycophenolate (MMF) and Methotrexate, demonstrated no significant difference between the both. However, the time to failure was higher in MMF arm as compared to Methotrexate (6). Other than this, a prospective open label trial observed that a regimen of parenteral methotrexate followed by oral methotrexate showed improvement in ITAS scores at end of 24 weeks (7). In a different study, by Hoffman et al, although 13/16 patients achieved remission, 44% of them relapsed on tapering of steroids (8).

In view of higher risk of toxicity compared to other agents, cyclophosphamide is generally preferred in refractory patients. A meta-analysis of 10 observational studies revealed that 48% of patients had a partial response to the agent (7). A recent study in China observed that a low dose cyclophosphamide improved outcomes in a high-risk cohort (9).

Azathioprine has been studied in few studies of TA. In a study by Valsakumar et al, in a cohort of newly diagnosed patients, azathioprine showed improvement in terms of clinical, laboratory and angiographic parameters at 3 months of follow up (10).

There has been a lot of promising data on Mycophenolate in TA. Danda et al. in their cohort of 602 TA patients, had 251 patients with a follow up data of more than 12 months. One hundred and sixty (63%) of these patients had been on MMF. Compared to other DMARDS, numerically higher proportion of patients on MMF had sustained inactive disease, with no serious adverse events (11).

A prospective study in China, showed that Mycophenolate mofetil was effective in controlling disease activity and retarding angiographic progression with an effective rate of 80% (12).

BIOLOGICAL DMARDS

1) Tocilizumab

A phase III Randomized controlled study, TAKT, randomized 36 patients to receive either Tocilizumab or placebo with background corticosteroids. They demonstrated that the time to relapse was longer in TCZ group compared to control group, however this was not statistically significant (13). A long-term extension of this study demonstrated that patients on weekly sub cutaneous TCZ had clinical improvement and radiological stabilization at 96 weeks of follow up (14).

In a study by Goel et al, 10 difficult to treat patient of TAK received Tocilizumab, and although all 10 of them responded initially, the benefit was not sustained on stopping Tocilizumab (15).

In a systematic review and meta-analysis of 17 observational studies with 222 patients receiving TCZ treatment, it was revealed that 87% achieved at least a partial clinical remission, 88% achieved angiographic stabilization, 62 % had reduced uptake on PET-CT and 94% had reduction in acute phase reactants. Patients on TCZ were able to reduce the median prednisolone dose by 83% (16).

2) Tumour necrosis factor inhibitors

A review article documented 13 studies with 96 TA patients who were treated with TNF inhibitors (infliximab, etanercept and adalimumab). Clinical improvement was reported in 61%, Glucocorticoids were stopped in 39%, and 3 patients showed regression of lesions on MR angiography. Twenty-eight relapses were reported in a follow up of 24 months (17).

A point of concern with TNF inhibitors, however is the high risk of tuberculosis, especially in endemic countries like India.

3) Rituximab

Results for Rituximab are conflicting with a retrospective study demonstrating persistent disease in 4/7 patients. In contrast, multiple case reports showed a positive response (17).

ORAL SMALL MOLECULES

Tofacitinib

Multiple Case reports have been published recently, where, patients with TA who did not respond to csDMARDs, TNF inhibitors or tocilizumab, had good clinical and imaging responses with Tofacitinib at a dose of 5 mg twice a day (18,19,20). Kong et al. in their prospective observational study of 53 patients, compared efficacy of tofacitinib vs. methotrexate (with tapering glucocorticoids in both groups) over a period of 12 months. At 6 months and 12 months, tofacitinib group had a higher complete remission rate and fewer relapses (21).

Endovascular and surgical interventions

The main indications for interventions in TA include critical ischemia with risk of end organ damage, uncontrolled hypertension, coarctation of aorta, aortic aneurysm, and aortic regurgitation. Interventions should ideally be performed during periods of remission, as the complication rate and mortality is higher when the disease is active. Interventions include balloon dilatation/ stenting. In cases of aortic aneurysms, Bentall's procedure for aortic regurgitation and TEVAR (Thoracic endovascular repair), procedures can be used (22).

Prognosis

Survival rate at 5 years, ranges from 67–100 % in various studies (23,24). A recent population-based study from Korea comprising 2,731 TA patients, the 10-year survival rate was 85% (154). A French multi-centre study a 96% overall survival rate at 10 years. The survival and mortality rates varied depending on ethnicity and have improved with time (25). Poor prognostic factors affecting survival are progressive disease course, thoracic aorta involvement and retinopathy (25). Mortality rates range from 3–21%, and the most common causes of death are heart failure, stroke, infections, and post operational complications

CONCLUSION

TA is a difficult disease to manage, with considerable controversy in differentiating activity from damage. GC forms the mainstay of medical therapy with upfront initiation of steroid

sparing agents. Conventional DMARDs such as methotrexate, azathioprine, MMF, and cyclophosphamide are commonly used as steroid-sparing agents, although the evidence for their use is based on small case series. Amongst all the cDMARDs, MMF appears to be the most promising, as it is safe and highly effective in controlling disease activity in TA.

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APPROACH TO INFLAMMATORY ARTHRITIS

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Inflammatory arthritis is the most common presentation noted in rheumatological clinics. Most of these patients are often times first seen in primary health care setting. It is imperative that all physicians be aware of the possible presentations and differentials as it would help guide these patients for early diagnosis and treatment. In India prevalence of RA is estimated to be 0.7% where as the global prevalence is 0.46%.[1] Rheumatological disorders evolve over time. Some of the arthritis presenting to a physician might be a component of connective tissue diseases like systemic lupus erythematosus. Detailed clinical history and physical examination help us identify the appropriate investigations and initiation of timely management. Rheumatoid arthritis awareness day is observed on February 2nd, the theme for year 2024 is “Living well with RA: Early diagnosis, Effective Management and a Brighter Future”

1. What is Inflammatory arthritis?

Inflammatory arthritis is the painful inflammation and stiffness of the joints. Peripheral arthropathies can be inflammatory or degenerative in nature. Before we evaluate the probable cause for arthritis, it is a must to confirm that the presenting pain is due to an

articular involvement. Regional pain can arise from joints, periarticular structures, bone, muscle, fascia or nerves.[2]

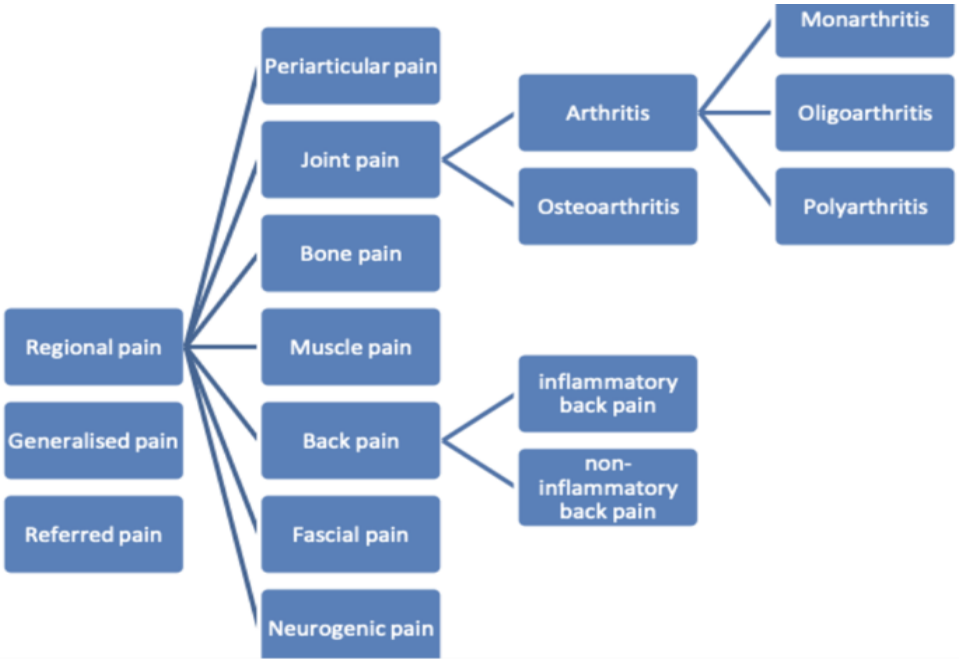

Fig. 1: Main Rheumatological Patterns

Step1 : Recognise that it is an articular syndrome.

If the pain is arising from a joint, pain will show pain in all movements. Both active and passive movements will be similarly affected. Joint movement is often limited owing to swelling or structural damage. Resisted movements performed on the joint do not exacerbate the pain (as expected since the joint is not moved by such manoeuvres).

Affected joints are often tender on palpation along the joint margins. When coarse crepitus, capsular swelling, effusion and/or deformity are also present, this makes involvement of the joint more obvious. Increased articular warmth also indicates intra-articular inflammation, but caution should be exercised to distinguish extra-articular local inflammation, such as in cellulitis overlying a joint

Each joint involved in the musculoskeletal system needs to be examined diligently and the number of tender joints and swollen joints needs to be documented at presentation and at follow up.

Step 2: Identify the three fundamental features of the articular pattern:

A. ‘Inflammatory’ or ‘non-inflammatory’ nature of the disorder;

B. The temporal pattern of the disorder; especially acute versus chronic duration;

C. The spatial pattern: primarily, mono-, oligo- or polyarticular involvement

The most important goal is to differentiate the features of joint damage, predominantly caused by osteoarthritis (OA), from those of inflammatory joint disease. Medical history and physical examination are critical in this respect.

Inflammatory arthritis can be distinguished by the presence of these characteristic features:

- Joint pain is worst in the morning and is relieved as patients get up and start to move their joints.
- Morning stiffness is often prolonged, lasting for more than 30 min and sometimes for several hours.
- Stiffness after rest may persist for more than 5 min.
- Patient may additionally complain of non-specific features like fatiguability, weight loss, night sweats, low mood, and irritability.

In inflammatory diseases, the synovium becomes inflamed, engorged, and eventually hypertrophied and the volume of synovial fluid increases. This increase in soft tissue and fluid occurs within the limiting confines of the capsule and can increase the pressure within the joint causing pain, stiffness, and restriction of movement. A joint with increased intra-articular pressure is most comfortable in the position that minimises the pressure. This position in mild-mid flexion is called loose pack position (capsule is loose). Inflammatory arthritis is also marked by the spontaneous flares that occur in a well controlled arthritis patient.

Universal Stress pain

The most sensitive sign of synovitis, occurring even before there is visible swelling or restricted movement is the universal stress pain. The joint that is examined does not reveal any tenderness in neutral position, however pain can be elicited in extremes of range of movements like full extension and full flexion. Joint damage is associated with a more even spread of pain throughout the range of movement.

2. What are the patterns of inflammatory arthritis?

Inflammatory arthritis can be monoarticular when it affects a single joint, oligo-articular when it affect 2-4 joints and polyarticular when it affects 5 or more joints. Based on the duration of symptoms, number of joints involved and presence or absence of symptoms suggestive of inflammatory arthritis, the possible differential diagnosis are summarised in Fig. 2[3]

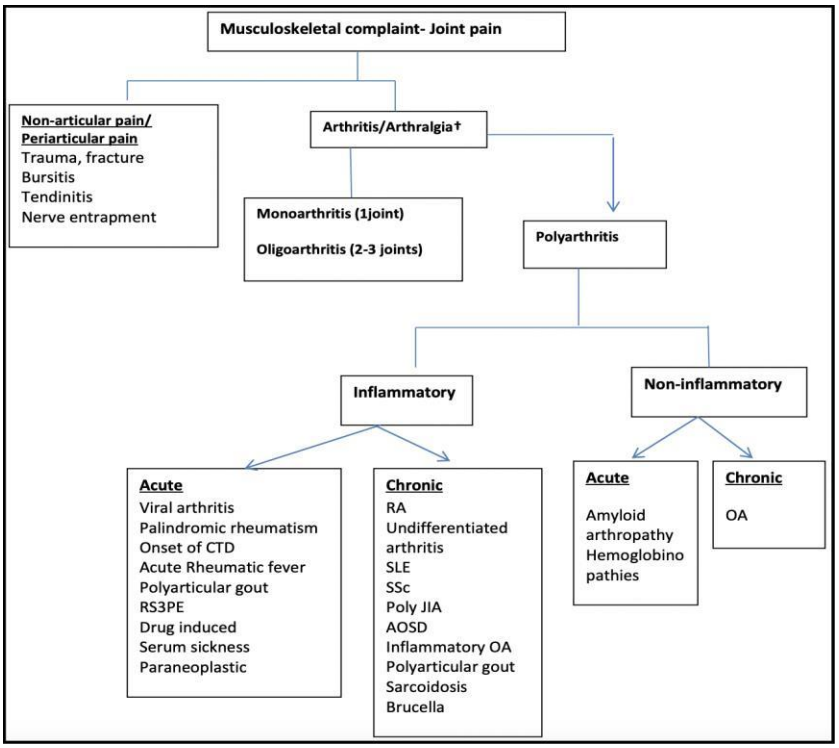

Fig. 2: Approach to a patient with joint pain with differential diagnosis

Some of the other features that need to be observed are whether the joint involvement are:

- Symmetrical v/s asymmetrical

- Additive v/s migratory
- Involvement of small joints v/s large joints v/s both
- With or without inflammatory back pain
- With or without other systemic manifestations.

APPROACH TO A PATIENT WITH INFLAMMATORY ARTHRITIS?

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Monoarthritis:

The most common causes of acute inflammatory monoarthritis are

- crystal synovitis,
- septic arthritis

Crystal synovitis has the following characteristics:

- rapid onset of pain and swelling—at its worst within 6–24 hours of pain onset;
- severe pain—often described as 'worst ever';
- marked tenderness—often unable to bear clothes or bed sheets touching the overlying skin;
- often florid synovitis with a tense effusion, adjacent soft tissue swelling and overlying erythema;
- the episode is self-limiting, even without treatment, over a few days or a few weeks.

Crystal Arthropathies

Gout is the most common cause of crystal synovitis. The first episode often starts at night and involve the first metatarsophalangeal joint, although any extremity joint may be involved. Can occur spontaneously, but recognised provoking factors include local trauma to the joint and intercurrent illness or surgery. Systemic symptoms such as fever and malaise may be present. Initial episodes of gout almost always follow a monoarticular recurrent pattern with symptom-free intervals, predominantly in the lower limbs. With time, intervals become shorter, the upper limbs also become involved and more than one joint can be affected in each episode, occasionally leading to a polyarticular pattern.

Acute calcium pyrophosphate (CPP) crystal arthritis ('pseudogout') presents a similar clinical picture. It is however mainly restricted to patients over the age of 60 years and particularly targets the knee. Other common sites are the wrist, shoulder, and ankle, although almost any joint can be affected. Definitive diagnosis requires demonstration of sodium urate or CPP crystals in aspirated synovial fluid.

Septic arthritis

The classic presentation of septic arthritis involves the acute or subacute onset of pain, swelling and sometimes erythema in a single joint. Symptoms and signs are progressive from day to day and do not plateau in the first 24 hours. Systemic symptoms such as fever and malaise may be present. RA and immunocompromised status (e.g., diabetes) are risk factors and sepsis should always be considered in a patient with RA who reports a 'flare' in just one or two adjacent joints. If the diagnosis is strongly suspected, the patient requires immediate admission and treatment for sepsis pending the results of synovial fluid and blood cultures—it is a medical emergency.

Other causes of acute monoarthritis include

- post-traumatic synovitis,
- palindromic rheumatism,
- reactive arthritis,
- psoriatic arthritis, and

- bacterial endocarditis.

Chronic monoarthritis:

The main possible causes of chronic inflammatory monoarthritis include infection (Mycobacterium, Brucella, Borreliosis, others), monoarticular presentation of oligo- or polyarthritis (juvenile idiopathic arthritis, reactive arthritis, seronegative spondyloarthropathy) and a foreign body (e.g., plant thorns). The most common infectious cause of chronic mono arthritis is tuberculosis.[4] Tuberculosis should always be ruled out in a chronic mono arthritis case. Differential diagnosis must incorporate causes of non-inflammatory arthropathy, such as OA, recurrent hydrarthrosis, osteonecrosis, chronic regional pain syndrome, neuropathic (Charcot's) joints and tumours, including pigmented villonodular synovitis.

Oligoarthritis

Oligoarthritis describes joint inflammation affecting two to four joints. Synovitis (esp. of asymmetrical distribution), with adjacent periarticular inflammation (eg. dactylitis) is strongly suggestive of seronegative spondyloarthropathy. Inflammatory back pain is a typical sign of axial spondyloarthritis. Inflammatory back pain is distinguishable by the presence of severe back pain early in the morning, sometimes awakening from sleep and improving after exercise/movement.

Reactive arthritis or arthritis associated with inflammatory bowel disease may show oligoarthritis. LOOK FOR: presence of inflammatory low back pain, a personal or family history of psoriasis, inflammatory bowel disease, AS, uveitis and the occurrence of any infectious disease (infectious diarrhoea, urinary tract infection) in the weeks preceding arthritis

Other causes of Oligoarthritis

RA, juvenile idiopathic arthritis, oligoarticular gout, OA with CPP deposition and Behçet's disease. Löfgren's syndrome is a type of acute sarcoidosis that is most accompanied by bilateral ankle arthritis, fever, and erythema nodosum, especially of the legs. Polymyalgia rheumatica, patient is typically an elderly, presenting with pain and stiffness in the neck, shoulders, and hip girdle due to inflammation that mainly affects the periarticular structures

(tenosynovial sheaths, bursae). Malaise, fever, fatigue, anorexia, and weight loss are common features. Jaw claudication, temporal headaches and loss of vision suggest concurrent temporal arteritis and warrants immediate attention to prevent vision loss.

Polyarthritis

Polyarthritis describes joint inflammation involving, simultaneously, five or more joints, if present for more than 6 weeks it is defined as chronic in addition. The most common cause for this pattern is RA. In RA small joints of the hands and feet are predominantly affected, but also large joints may be involved symmetrical and are additive i.e., added progressively. There is no inflammatory low back pain. Onset of especially aggressive disease may be accompanied by constitutional features such as fever and lymphadenopathy. Other systemic manifestations may occur but tend to occur later in the course of disease.

Differential diagnosis for **chronic polyarthritis** include juvenile idiopathic arthritis connective tissue diseases, such as SLE, primary Sjögren's syndrome, and mixed connective tissue disease (MCTD).

Psoriatic arthritis can also present with polyarthritis, more asymmetrical and involve either the distal interphalangeal or the sacroiliac joints. Chronic sarcoid arthropathy may evolve with polyarthritis. OA with CPP crystal deposition deserves consideration, especially in older patients; a pre- existing pattern of generalised OA with recurrent inflammatory episodes may suggest this condition. Chronic polyarticular gout may have a similar pattern of distribution. Viral arthritis, associated with parvovirus B19, HIV and hepatitis, may present as polyarthritis, but tends to have a more acute onset than RA or the connective tissue diseases. Still's disease (in adults or children) is characterised by an acute or subacute onset of arthritis, associated with fever, evanescent skin rash, weight loss, lymphadenopathy and/or splenomegaly.

Recurrent episodes of polyarthritis – but also mono- and oligoarthritis - with fever point to the diagnosis of rare hereditary disorders. Recurrent inflammatory episodes, characterised by as fever, abdominal pain, diarrhoea, rash, or arthralgia. Between the fever episodes, patients with most of these syndromes generally feel healthy and function normally. These

syndromes include familial Mediterranean fever, cryopyrin-associated periodic syndrome and others.

Main systemic manifestations associated with rheumatic diseases

Systemic manifestations seen in polyarthritis that warrant detailed evaluation include :

- Skin involvement like photosensitive rash, alopecia, purpura, vasculitic rashes, sclerodactyly, telangiectasia, Heliotrope rash, Gottron's papules, Raynaud's phenomenon, psoriasis.
- Mucosal manifestations like oral ulcers, genital ulcers, dry eyes and dry mouth, serositis, uveitis, scleritis, episcleritis
- Arterial or venous thromboembolism
- Dysphagia
- Dyspnoea
- Recurrent abortions
- Muscle weakness
- Convulsions, psychosis, peripheral neuropathy
- ENT manifestations like sinusitis, deafness, otitis media

4. What are the investigations needed?

Routine investigations evaluating hemogram, liver and renal functions are essential. Inflammatory parameters like erythrocyte sedimentation rate, c-reactive protein help guide the treatment. These are not reliable in certain conditions like SLE. Serological factors like rheumatoid factor (RF), anti cyclic citrullinated peptide (Anti CCP), antinuclear antibodies (ANA), ANA profile, anti neutrophil cytoplasmic antibody (ANCA), viral antibodies are required to be evaluated based on the clinical picture of the patient. Physicians should refrain from using these tests as screening tool for rheumatological disorders. Ordering a battery of laboratory tests will often result in information noise. It would plainly add to the cost of healthcare and not to help clarifying the diagnosis.

Synovial fluid analysis, along with cultures is essential to differentiate the causes for acute mono-arthritis.

Radiographs are of importance in chronic polyarthritis. It helps identify soft tissue swelling, juxta-articular osteopenia, joint space narrowing and bone erosions. In an acute setting especially with history of trauma, it is advisable to consider radiographs to rule out fractures.

Ultrasonography is being increasingly used in the field of rheumatology off late and helps in identifying synovitis in ambiguous cases. It has an advantage of being able to evaluate bone as well as soft tissues and with no ionising radiation, hence allowing for repeated use. It is sensitive in detecting synovitis and joint effusion. It can also aid in guided aspiration of synovial fluid. Adding Power Doppler can help us identify the presence of inflammation in the joint. Magnetic Resonance Imaging (MRI) may be required to evaluate some marrow edema in suspected cases of spondyloarthropathy presenting as oligoarthritis. However, caution must be exercised while requesting the imaging and consider it only in a setting where it adds to clarifying the diagnosis or will alter the treatment

WHEN TO CONSULT A RHEUMATOLOGIST?

Table 1 provides a summary on categorising the patients into low risk (green), moderate risk (amber) and high risk (red). It is important to identify the need for the high risk patient to be seen by a rheumatologist on priority basis to prevent mortality and morbidity. Keeping patients of moderate risk on high radar and sending over for a consultation is advisable. Low risk patients require a consult if symptoms are persistent or if they move to the moderate risk category overtime.

Insidious onset	Slow Progression	Pyrexia, Loss of Weight
No joint involvement	Variable joint involvement	Significant Rash Lymphadenopathy
One or few joints (<5)	Regional pain, discomfort, moderate debility	Vital organ involvement Unbearable pain and debility

Dull ache and pain, mainly localised	Moderately elevated ESR CRP	Weakness and Malaise Vasculitic manifestations
Normal ESR, Normal CRP		Multisystem involvement
No significant disability		High ESR, CRP

Table 1: Categorising patients as low, moderate and high risk

Need for early diagnosis and treatment

There multiple studies that have reiterated the fact that identifying rheumatological disorders early and initiating adequate treatment in the early presentation results in better outcome. Rheumatology consultation <12 weeks from the onset of symptoms is essential as this is considered the therapeutic window of opportunity. European Alliance of Associations for Rheumatology (EULAR) recommends that any patient with joint pain, associated with swelling/effusion should be seen by a rheumatologist within 6 weeks.[5] Delay in diagnosis and initiation of treatment or providing inadequate treatment results in poor disease outcome with possibility of deformities and significantly affects the quality of life in such patients.[6]

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REACTIVE ARTHRITIS

What's new: Quick run

- *Reiter's Syndrome* is now more appropriately called Reactive arthritis (ReA).
- The triad of arthritis, urethritis and conjunctivitis occurs only a minority of patients (<20%) with ReA.
- ReA is now considered a part of the spectrum of Spondyloarthritis (seronegative arthropathies)
- The role of MHC gene HLA-B27 (classically associated with Ankylosing Spondylitis) is now recognised in the pathophysiology of ReA.
- *Chlamydia trachomatis* is now known to be the most common genitourinary infection leading to ReA.
- Broad spectrum antibiotics have no efficacy in the treatment of ReA, unless there is a proven active infection (genitourinary or gastrointestinal)

Introduction

"*A youth does not suffer from gout until after sexual intercourse"* – this line from 4th century BC text by Hippocrates most likely described florid synovitis occurring after a genitourinary

infection post sexual exposure – now deemed Reactive arthritis (ReA). Gout was used to describe any acute severe arthritis at that time. Subsequently, references to a post infectious (genitourinary or gastrointestinal) acute arthritis with associated features were described by Christopher Columbus who wrote about himself - *"I have never had such affliction of my eyes with hemorrhage and pain as in this time".* He was at one time 'paralyzed and bedridden" due to 'gout' – again a misnomer running upto the Renaissance age. The usage of the term 'Reiter's syndrome' was suggested by authors Panush, Wallace and Engleman 80 yrs ago, which they voluntarily retracted in 2007 in the light of war crimes and inhumane experiments attributed to Prof.Hans Reiter who was a member of the German Nazi Party and director of the infamous Kaiser Wilhelm Institute of Experimental Therapy. Today, ReA is the term that is used to encompass a heterogenous multisystem syndrome that is due to an aberrant autoimmune response to gastrointestinal (GI) or genitourinary (GU) infections.

Etiology

ReA is triggered by a bacterial infection, often of the GI or GU tract. Common pathogens associated with the development of ReA are listed below.

Genitourinary	Gastrointestinal	Others
Chlamydia trachomatis *Neisseria gonorrohea* *Mycoplasma hominis* *Ureaplasma urealyticum*	*Salmonella enteriditis* *Shigella spp.* *Yersinia enterocolitica* *Campylobacter jejuni*	BCG vaccine therapy for bladder cancer COVID-19 vaccination Post-streptococcal tonsillitis HIV infection

Epidemiology and pathophysiology

Often afflicting predominantly young adult males in the second and third decades of their life, ReA can occur at any age. Pediatric ReA (age <10yrs) is relatively rare. The incidence is estimated to be 3% after GU infections and 8% after GI infections with the incriminating pathogens.

There is ample evidence to suggest that ReA is an immune-mediated syndrome triggered in a genetically predisposed individual by a recent remote infection. The genetic component is exemplified by HLA-B27, a gene of the MHC complex , which is estimated to occur in

approximately 50% of ReA patients. The presence of HLA-B27 potentiates the presentation of bacterial antigens to T cells, altering self-tolerance of the host immune system and leading to an inflammatory cascade manifesting into the clinical syndrome of rheumatic proportions. The reader has to be cautioned that the mere presence of HLA-B27 does not establish the diagnosis of ReA.

A remote infection (GI or GU) induces T lymphocytes to get activated by lipopolysaccharides (LPS) and nucleic acids which then translocate to various organs (joints, conjunctiva, skin, uvea) where they mount an inflammatory response to self tissues with an objective of clearing these molecules. The resultant clinical picture is that of florid inflammation in the involved organs.

Clinical manifestations

Symptoms develop 2 weeks on an average after the inciting infection. A good unhurried history is the only method of picking up a recent GI or a GU infection, since a majority of the patients are asymptomatic with respect to the original infection by the time they manifest ReA. History must include symptoms of urethritis, diarrhoea, recent sexual exposure and previous history of ReA. ReA can be self-limiting, recurrent or chronic (20%) lasting beyond 6 months.

The classic '*Reiter's triad*' encompassing urethritis, arthritis and conjunctivitis occurs in <20% of ReA patients. Further with the recognition of various other manifestations of the syndrome, the dependence on the presence of these features for a diagnosis has gone down. In view of the pathophysiology and clinical features closing resembling the spondyloarthritides, it is not surprising that ReA is now considered a part of the spectrum of these seronegative (meaning Rheumatoid factor AND anti-CCP negative) arthritides. The prominent clinical features are listed below with those in bold representing common manifestations:

- Musculoskeletal
    - **Oligoarthritis of large joints**, predominantly of the lower limbs
    - Polyarthitis with sausage digits (dactylitis)

- **Axial involvement with sacroiliitis**, lumbar spine facet joints
- **Enthesitis** (pain / swelling / tenderness of site of insertion of tendons and ligaments)

- Ocular
  - **Sterile conjunctivitis, Uveitis** (aggressive disease), Iritis

- GU symptoms
  - **Urethritis, cervicitis**, prostatitis and cystitis

- Dermatologic
  - **Keratoderma blenorrhagicum** (often seen in HIV positive individuals)
  - **Circinate balanitis**
  - **Aphthous ulcers**
  - Erythema nodosum

Lab Evaluation and Diagnosis

Investigation results in ReA are non-specific and currently there are no specific diagnostic tests that can establish the diagnosis of ReA. Hence, the diagnosis is clinical with the central theme being the temporal relationship between an infectious episode preceding the clinical manifestations described above. American College of Rheumatology criteria for the diagnosis of ReA (1999) do exist but have been often criticised for the lack of sensitivity.

- Evaluation for the preceding infection
  - GI infections almost always resolve by the time ReA manifest. Hence, stool testing is of no significant benefit unless the patient has persistent intestinal symptoms

- GU infections: *Chlamydia trachomatis* DNA PCR can be done from urine samples and or urethral swabs, but availability is an issue. HIV testing is recommended in all patients with a diagnosis of new onser ReA. Routine urine cultures are not indicated.

- Evaluation of the ReA manifestations

    - Joint fluid aspiration may help in distinguishing from septic arthritis, especially in cases of monoarthritis. Oligo and polyarticular manifestations are seldom due to septic arthritis.

    - Ophthalmological evaluation is indicated even if the patient has mild ocular symptoms since uveitis in ReA can be rapidly progressive leading to morbid sequelae and vision threatening complications

    - Leucocytosis with neutrophilia with raised ESR and CRP are common and are *not always* suggestive of active infection at the time of the diagnosis.

Treatment and Prognosis

There is strong evidence *against* the efficacy of broad-spectrum antibiotic therapy in ReA. Hence, other than in cases where active GU infections like Chlamydia or HIV have been demonstrated, there is no indication for treatment with antibiotics. NSAIDs have been the mainstay of therapy with majority of patients requiring dosages bordering the upper limits (eg: Naproxen 500mg BD or Etoricoxib 120mg OD). Drugs may be withdrawn once symptomatic improvement occurs and inflammatory parameters show resolution but this may require two to three weeks of therapy. Intra-articular injections of triamcinolone or methyprednisolone are an alternative where one or two large joints are involved. Oral corticosteroids (Prednisolone or equivalent) are often a choice of the desperate rheumatologist trying to warp time to faster recovery and can often be avoided. Physiotherapeutic exercises should be considered in all patients since involvement of the knee and hips joints can lead to rapid atrophy of the thigh muscles.

DMARDs (sulfasalazine, methotrexate and others) are indicated in chronic synovitis (lasting >6 months) or in patients who have recurrent or persisitent ocular manifestations. Newer therapies include biologics (anti-TNF, anti-IL17 therapy) in refractory patients.

Majority of the ReA (80%) patients show complete recovery by the end of 3-4 months. Recurrent or chronic disease is more often seen in HLA-B27 positive patients. With appropriate DMARD and immunomodulatory therapy, the inflammatory disease can be well controlled with the expectation of near normal life for majority of the patients.

Conclusion

With the recognition of the protean manifestations of ReA, the old school image of the Reiter's triad has been replaced with a spondyloarthritic concept with genetic background being increasingly recognised. A disease that has perplexed medical men for millennia still retains its aces in the game and the show of cards is unlikely to happen in the near future.

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HOW TO EFFECTIVELY USE LABORATORY INVESTIGATIONS IN RHEUMATOLOGY

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The topic is important and confusing at the same time. Since there are so many investigations and most of them overlap each other, we have to be sure what we want the laboratories to test and how do we wish them to be tested. Laboratory investigation in Rheumatology are like an arrow once left we wait for it to hit the target and if it doesn't we wonder what to do next.

First step for sending any investigation is to come to a differential diagnosis in our OPD. The differential diagnosis can be reached via a good history and a thorough clinical examination. Understanding the two terms Sensitivity and Specificity is key in choosing the required tests.

Sensitivity is how good the test is in correctly identifying people who have the disease that is it rules in the disease e.g ANA.

Specificity is how good the test is to say that the person in fine that is it rules out the disease e.g dsDNA.

First in any patient we start with the basics Complete blood count, C reactive protein, RFT, LFT, urine analysis.

CRP is not sensitive to changes in SLE activity and is unaffected by age and gender so to differentiate between a flare or an infection can be used effectively.

RHEUMATOID FACTOR(RF)

It's an anti-immunoglobulin antibody, Igm against Fc portion of Immunoglobulin. It's a very nonspecific test. Levels do matter though; high levels indicate worse prognosis i.e the patient is more likely to get joint erosions and deformities. It may also be positive in healthy control subjects upto 1% in young people and upto 5% in individuals more than 70yrs. It has a sensitivity of 50% and specificity of 90%. A diagnosis of Rheumatoid arthritis (RA) can't be confirmed with a positive test nor can we exclude RA with a negative test.

Diseases with elevated RF

1. RA
2. SLE
3. Sjogren syndrome
4. Interstitial pulmonary fibrosis
5. Infectious mononucleosis
6. TB
7. Infective endocarditis (minor criteria)

CLINICAL SIGNIFICANCE

1. Positive in 80% patients with RA.
2. Around 15%-20% RA never have RF positive.
3. High levels in plasma indicate worse prognosis.

ANTI CITRULLINATED PROTEIN ANTIBODY (ACPA)

It is Specific for RA (95%-98%). It is rare in other conditions. Sensitivity is around 30% to 60%. Positive test helps in diagnosis but negative test doesn't rule out RA. ACPAs are also associated with RA related interstitial lung disease and cardiovascular disease.

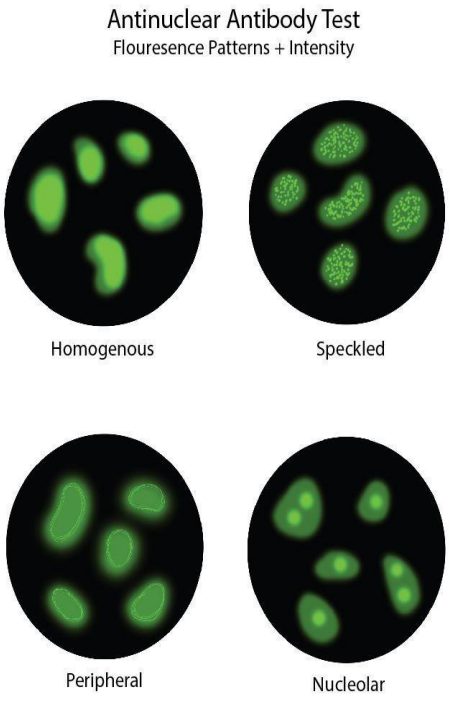
Clinical importance:

1. If both RF and ACPA are positive in early undifferentiated arthritis, the risk of progression to RA is almost 100%.
2. More than 1/3 patients with RA maybe negative for both antibodies.
3. Both RF/ACPA maybe present several years before clinical symptoms of RA can be seen. Risk of developing RA for asymptomatic individuals who are RF positive depends on-

- RF titre
- Positive family history in first degree relative
- Co presence of ACPA

ANTI NUCLEAR ANTOBODIES (ANA)

They are antibodies that attack components of the nucleus, binding to DNA, RNA, nuclear proteins or nucleic acid complexes. They are very sensitive and not specific. They can be done by indirect immunofluorescence (IIF) which is more sensitive or ELISA.IIF is reported as titres e.g 1:80, 1:160 and so on. Titres higher than 1:80 are considered positive. Higher the titre more likely you have an autoimmune disease. ANAs are also seen in healthy normal people but as titres increase positivity rate in normal individuals decreases e.g ≥1:40 seen in 20 to 30% whereas ≥1:320 seen in 3% normal people. IIF also reports patterns. Patterns may or may not point to a particular disease.



Diseases having positive ANAs:

SLE

Drug induced lupus

Mixed connective tissue diseases

Scleroderma

Sjogren syndrome

Dermatomyositis/Polymyositis

RA

ANA may also be positive in a few non rheumatological diseases like Hashimotos thyroiditis 40%-50%, autoimmune hepatitis 60%-90% as also in chronic infectious diseases like Hepatitis C, infectious mononucleosis, Tuberculosis

Clinical significance:

- Negative ANA rules out lupus.
- Titres don't co relate with disease activity.
- Once ANA is positive there is no need to repeat the test.

- 1 in 9 healthy women have a positive ANA.
- Sometimes patterns don't correlate with the disease.

EXTRACTABLE NUCLEAR ANTIGENS

1. **dsDNA**- Is highly Specific for SLE. It correlates with disease activity. It helps to monitor lupus nephritis. Its absent in drug induced lupus
2. **anti Smith antigen: snRNP** (small nuclear ribonucleoprotein). It is again specific for lupus. The levels do not fluctuate with disease activity

Specific ANAs

- Anti dsDNA/Anti Sm – SLE.
- Anti histone- seen in >95% cases of Drug induced lupus.
- Ant ribosomal P- neuropsychiatric manifestations and renal disease.
- U1-RNP - Present in SLE (30%-40%), high titres in MCTD.
- Anti centromere- limited Scleroderma (CREST). Increased risk of PAH. Good prognosis
- Anti RNA polymerase 3- Scleroderma kidney
- Anti Scl 70/Anti topoisomerase 1- Systemic sclerosis. ILD. Bad prognosis
- Anti SSA/Ro, Anti SSB/La- SLE, Sjogren syndrome
- ant histidyl-tRNA synthetase (Anti Jo-1) Polymyositis. Higher risk of ILD
- anti–Mi-2-associated with dermatologic manifestations

ANTI PHOSPHOLIPID ANTIBODIES

Anti cardiolipin antibodies (ACLA)

- May be targeted against beta2 glycoprotein I (beta 2GPI) that is bound to cardiolipin or to cardiolipins themselves.
- Cardiolipins are found on cell membranes and platelets.
- Antibodies against cardiolipins are mostly transient a/w drugs, infections, cancer.

- May be IgG, IgM, IgA. IgG is most significant.
- Beta 2GPI that is not bound to cardiolipins can be detected separately.
- Result is considered significant when the titres are medium to high.
- Low titres of aCL or anti beta 2GPI IgM antibodies are present in 1% to 5% of healthy people.

Lupus anticoagulant (LA)

- Class of imunoglobulins against phospholipids, prothrombin and beta 2 GPI which inhibit phospholipid-dependent coagulation in vitro.
- Can cause prolonged aPTT.

Indications to do the test

- Unprovoked DVT or Pulmonary embolism
- Ischemic stroke under 50yrs
- Both arterial and venous events
- Recurrent thrombosis
- Thrombosis in an unusual site
- Pregnancy morbidity
- All patients with SLE

Clinical significance:

- Association with thrombosis is strongest for LA.
- Triple positivity is a/w higher risk of thrombosis with 10year cumulative incidence of 37.1% for first thrombotic event and 44.2% for recurrent thrombosis.
- Positive LA +/-moderate to high titre ACLA or anti beta 2 GPI IgM or IgG- high risk profile
- Moderate to high titre ACLA or anti beta 2 GPI IgM or IgG- moderate risk profile

- Low titre ACLA or anti beta 2 GPI IgM or IgG- low risk profile may not be a/w thrombosis
- Frequency of antiphospholipid antibodies is ≈ 13.5% in patients with stroke, 11% with MI, 9.5% with DVT, and 6% with pregnancy morbidity.

COMPLEMENTS

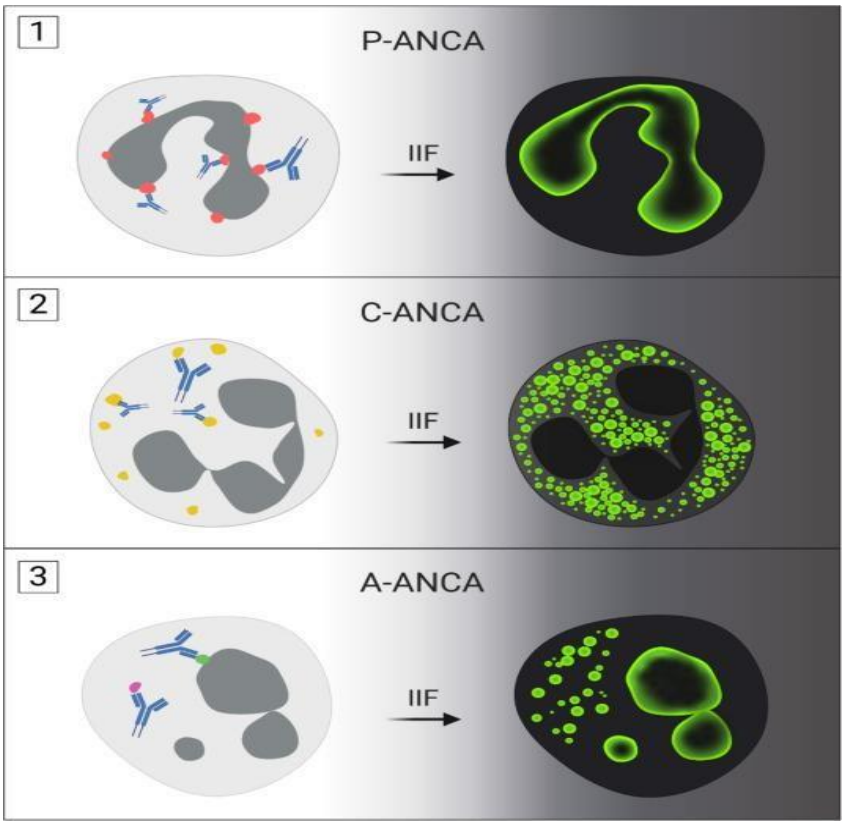
They complement the antibodies and phagocytic cells. They can be activated via two pathways, classical pathway (Ag-Ab complex) or alternative pathway (Bacterial endotoxin). Low complements can be seen in genetic deficiency, under production or over consumption of complements.

- Under production- eclampsia, HELLP.
- Over consumption- SLE, membranoproliferative glomerulonephritis, cryoglobulinemia, endocarditis, vasculitis, RA.

Low C3 can be seen in both classical and alternative pathway activation while low C4 only classical pathway e.g SLE

ANTI NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA)

They are predominantly IgG antibodies against cytoplasm of neutrophils and monocytes. Can be categorized as perinuclear ANCA(p-ANCA), cytoplasmic ANCA(c-ANCA) and atypical ANCA. Myeloperoxidase (MPO) and proteinase 3(PR3) are the major autoantigens. ELISA – detects anti PR3, anti MPO. Its more accurate with a higher positive predictive value (PPV). IIF- less accurate and has a lower PPV. The primary screening method should be an antigen specific assay. p-ANCA immunofluorescence has poor specificity for ANCA associated vasculitis (AAV), whereas anti-MPO antibodies have high specificity for AAV. The specificity with different antigen specific immunoassays was 98% to 99% for PR3-ANCA and 96% to 99% for MPO-ANCA.



CLINICAL INDICATIONS TO TEST FOR ANCA

- Glomerulonephritis
- Pulmonary hemorrhage
- Multiple lung nodules
- Mononeuritis multiplex or unexplained peripheral neuropathy
- Cutaneous vasculitis especially with systemic features
- Scleritis
- Retroorbital mass
- Chronic destructive upper airway disease
- Chronic sinusitis or otitis
- Subglottic tracheal stenosis

CLINICAL SIGNIFICANCE

- It is associated with small vessel vasculitides like granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), drug induced ANCA associated vasculitis, RPGN.
- Doesn't correlate with disease activity.
- 11% TO 15% of patients with GPA and 8% to 24% with MPA tested negative for both PR3 and MPO
- A positive ANCA is not diagnostic of ANCA associated vasculitis
- Gold standard for ANCA associated vasculitis is Biopsy
- ANCA positivity (at onset as well as during remission) increases the risk of recurrence 4 or more times

HLAB27

- Present in more than 90% patients with axial disease
- Association with peripheral spondyloarthropathy is not that strong
- Risk factors for spinal involvement in psoriatic arthritis include severe peripheral arthritis and HLAB27 positivity.
- For reactive arthritis and IBD associated arthritis 75% patients may be positive.
- For PsA and uveitis 50% may be positive.
- Its seen in 9% healthy, asymptomatic individuals.
- HLA-B27 positivity and buttock pain are significant predictors of progression of undifferentiated Spondyloarthropathy to Ankylosing spondylitis or Psoriatic arthritis.

ARTHROCENTESIS

Synovial fluid aspiration forms an important investigation especially in case of monoarthritis. It helps to differentiate infective joint from an inflammatory one. The fluid should be sent for routine microscopic investigation, cultures both Aerobic and mycobacterial if indicated and also for polarized light study to look for uric acid crystals or other crystal arthropathies like CPPD.

To summarize Autoantibodies are confirmatory but rarely diagnostic in Rheumatological diseases. A good balance is needed between the clinical picture and interpreting the investigations. Pattern recognition is the key when so much information is out there. And last but not the least common things are always more common.

EITOPATHOLOGY AND MANIFESTATIONS OF IGG4 DISEASE

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Abstract

Immunoglobulin G4-related disease (Igg4RD) disease is a multiorgan progressive immune-mediated fibro inflammatory disease of unknown etiology with characteristic histopathologic features. It can affect any organ. It can be localized or can have multisystemic involvement. Since its discovery nearly two decades our understanding of its pathophysiology and clinical manifestations has grown substantially. The rare occurrence of the disease and its atypical manifestations have posed a diagnostic challenge among treating physicians. However, the great abundance of literature in 2003, has shed light on varied manifestations and has eased our understanding of the disease. B cells play a central role in the pathogenesis of the disease. CD4 + Cytotoxic and the T follicular cells also have recently been shown to play an important role in the propagation of the disease and induction of fibrogenic cytokines. Glucocorticoids and immunomodulators have significantly reduced the burden of the disease. Early diagnosis and treatment of this disease can prevent fibrosis and subsequent irreversible emphasizing the need for prompt recognition and accurate characterization of IgG4-RD

Introduction

IgG4 is a slow insidious onset progressive disease that can be locally destructive and rarely fatal if not diagnosed in time.[1,2] It is typified by chronic activation of the immune system and tissue fibrosis. [3] They tend to form mass-like lesions sometimes mimicking malignancy for example dacryoadenitis soft tissue expansion in the retroperitoneum or diffuse enlargement of the pancreas, leading to suspected pancreatic adenocarcinoma.[4] Most commonly it involves salivary glands, lacrimal glands, lymph nodes, pancreas, bile ducts, retroperitoneum, and the aorta. The chronicity of the disease and its response to immunosuppression most commonly steroids has made autoimmune origin a likely etiology.[5]

Epidemiology

The exact prevalence of IgG4 disease is unknown. Due to its diverse manifestations, lack of awareness, and recent discovery, it is under recognised and underreported. It has a male preponderance and usually affects the middle-aged to elderly population in their 5th to 7th decade.[6,7] However, cases among the pediatric age group being affected [8.] As per the Nationwide survey in Japan in 2009 it has an incidence of 0.28-1.08 % among one lakh population.[4]

Certain studies have shown among the patients with Igg4 disease most of them had blue-collar occupations with long-term exposure to various solvents, gases, etc had increased incidence of IgG4RD, indicating the possible role of environmental factors in the development of IgG4 RD.[9,10]

Pathogenesis

Igg4 disease was initially recognized and was considered unique due to the predominant humoral inflammatory response. In patients with IgG4-related disease, oligoclonal expansion of the IgG4 clones was sequenced in peripheral mononuclear cells and the tissue.[11]Further studies found that the circulating plasmablasts expressed phenotype of mature B cells with high expression of IgG4 predominantly and less of IgM. The immunoglobulin sequencing of the circulating plasmablasts revealed extensive somatic

hypermutation involving both the hypervariable and framework regions of immunoglobulin suggesting a probable involvement of T cells.[12]In a study on Igg4 patients treated with rituximab, the patients who had relapsed after one year of treatment had a resurgence of plasmablasts compared to the ones in remission.[13] Similarly, studies have shown a reduction in the number of IgG4 clones with glucocorticoid therapy[13]. Cytotoxic T cells have been associated with the pathogenesis of igg4 disease. $CD4^+$ cytotoxic T lymphocytes and a specific T follicular helper cell subset have been studied to promote and contribute to IgG4 isotype switching.The number of cTFH2 cells correlates with the number of organs involved, circulating plasmablast numbers and, serum concentrations of both IgG4 and IL-4.[14,15]

Histologically, its characterised by an irregular whorled pattern of fibrosis called as storiform fibrosis with dense lymphoplasmacytic infiltration. Obliterative phlebitis due to the destruction of wall and lumen of the veins is usually seen in some patients.[16] The findings of ≥50 IgG4+ plasma cells per high-power field and an IgG4+to IgG+ plasma cell ratio of >40% strongly support IgG4 disease.[16,17] However, the number of IgG4 positive plasma cells should be interpreted with caution in cases of chronic fibrotic stage where the number of Igg4 positive stained cells might be lower and also depends on the extent of the sample studied. In other cases like nasal cavities, sinuses or lymph nodes Igg4 positive plasma cells can be seen higher in number, where findings of increased IgG4+ plasma cells at these sites were not considered specific to contribute to the classification criteria for IgG4-RD. [18.]

Also, serum IgG4 levels have low specificity for the diagnosis of the disease and it may not necessarily correlate with the severity of the disease.[19] Hence the diagnosis must be done after considering clinical, serological, and radiological data and a specific histopathological context must accompany the immunostaining.

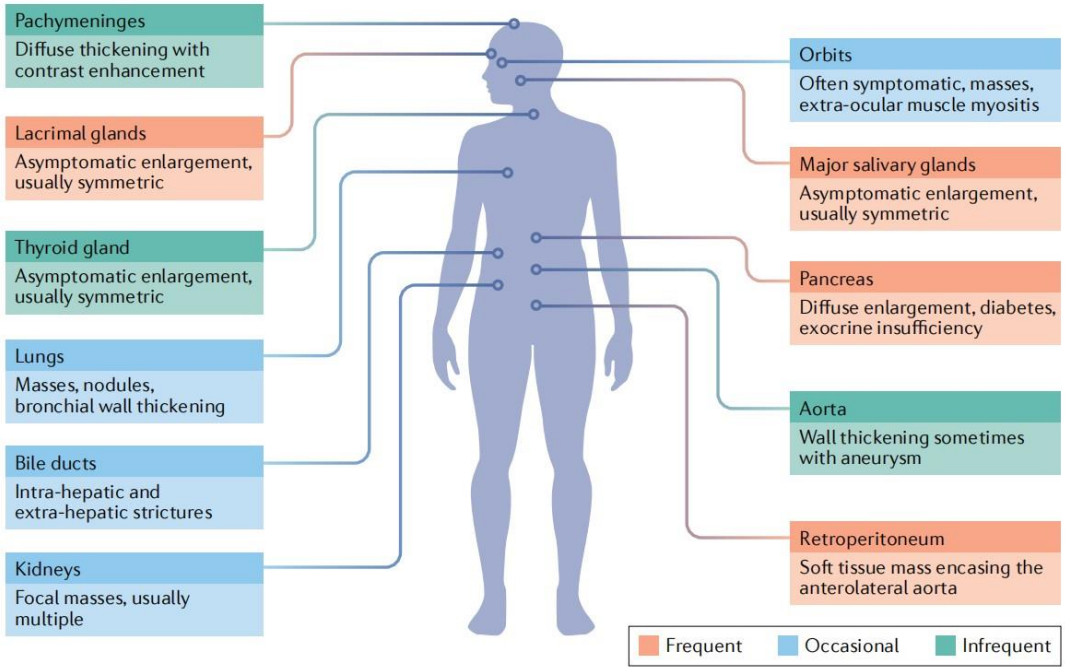
Clinical features

The clinical manifestations of IgG4-RD are usually tumor-like masses or organ enlargement, which result from dense tissue infiltration by immune cells and expansion of the extra-cellular matrix. There are 11 organs considered typical of IgG4-RD which include the pancreas, bile ducts, lacrimal glands, orbital tissues, salivary glands, lungs, kidneys, retroperitoneal tissues, aorta, meninges, and thyroid gland.[21]

Most patients have multiorgan involvement at diagnosis but tend to have one dominant phenotype. Acute fulminating infections do not occur in Igg4 disease. [19] In contrast to most other rheumatological diseases, IgG4 has insidious evolution. Patients can have subclinical symptoms from months to years before seeking medical evaluation, or at times go unrecognized. Incidental detection through imaging in cases of retroperitoneal fibrosis or aortitis is commonly reported. About 60% of patients with IgG RD have some degree of irreversible organ dysfunction due to a long latency period before clinical diagnosis.[17]

Some of the organs have characteristic radiologic imaging features for example sausage pancreas which is due to the capsular-like rim of edema surrounding diffusely enlarged pancreas, soft tissue encasement of anterolateral aspect of aorta in the background of retroperitoneal fibrosis, etc. [19]The clinical manifestations of 11 commonly involved organs are depicted in Figure 1

Figure 1 Schematic representation of typical organs involved and manifestations in Igg4 disease as per EULAR 2019 Classification criteria by Wallace et al [19,21]



Treatment and management

Being a fibroinflammatory disease, Glucocorticoids are typically the first-line treatment for IgG4-RD. However, relapse rates are higher when these drugs are tapered to low doses. They are used at higher doses at induction and are tapered slowly over weeks. Vital organ involvement requires higher initial dosing compared to other minor organ involvement. Studies have shown a substantial reduction in the number of activated cells and plasmablasts' response to treatment with glucocorticoids.[22,23] Due to long-standing disease and a need for chronic immunosuppression, steroid-sparing immunomodulators are usually advised for maintenance post-induction with steroids in the management of IgG4 disease. Low-dose cyclophosphamide and mycophenolate mofetil are all being used as steroid-sparing agents however the use of low-dose cyclophosphamide in clinical practice must be weighed against the potential long-term consequences well-established in other diseases.[24,25] Data on conventional disease-modifying drugs like methotrexate, hydroxychloroquine, and leflunomide are limited to case series, case reports, or retrospective studies.[26] Hence the use of these drugs and their efficacy in long-term

maintenance of IgG4RD in terms of decision-making is limited. B cell depletion therapy has proven to be excellent in the indication and long-term maintenance of IgG4 RD. In long-standing fibrotic disease through chronic, the use of anti-CD 20 antibody rituximab has shown good improvement.[26,] Rituximab has shown dramatic reduction in serum IgG4 levels, tissue myofibroblast activation, and cytotoxic t lymphocytes in IgG4RD. [27,28] Other B-cell targeting monoclonal antibodies like anti-CD19 are also being studied in the management of IgG4 disease. Recently a proof of concept study showed efficacy of abatacept in certain subset of patients with IgG4RD.[29] Newer therapies targeting different B cells, Cytotoxic lymphocytes, IL4, etc are being evaluated for the treatment of IgG4 RD.[30,31]

Conclusion and take home messages

IgG4-related disease (IgG4-RD) is a recently recognised chronic fibrotic inflammation, which can occur at any anatomical site. It often presents as a multiorgan disease and may be confused with malignancy, infection, or other immune-mediated diseases like Sjögren's syndrome or vasculitis. They can have manifestations ranging from visible organ swelling or organ dysfunction to asymptomatic incidental findings by imaging or biopsy. Although clinical, serologic, radiologic, and pathologic features all contribute to the classification of IgG4-RD, none of these approaches alone provides definitive evidence for the accurate classification of patients. Proper integration of data from all 4 domains of evidence must be taken into consideration for an accurate diagnosis of IgG4 disease. Glucocorticoids are the mainstay of therapy in IgG4 disease. Long-term treatment necessitates the addition of steroid-sparing immunomodulators. Prompt diagnosis and management can prevent irreversible organ damage and hence can avoid irreversible consequences .

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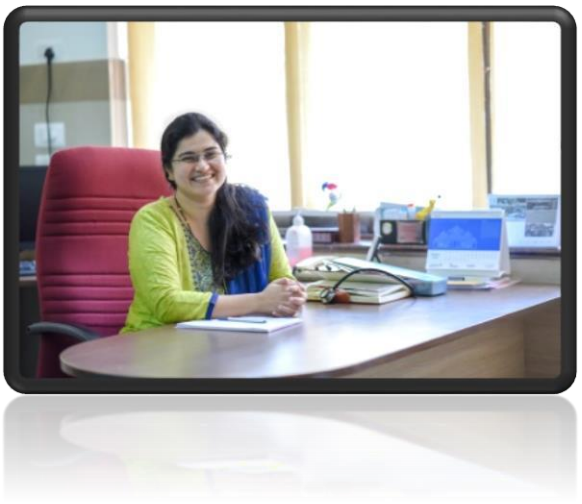
EMERGENCIES IN RHEUMATOLOGY



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Rheumatological illnesses can at times present as emergencies. These may be organ threatening or life threatening occurring due to disease process itself or infection. Prompt comprehensive initiation of treatment is of paramount importance in the management of these emergencies. Therefore, a thorough understanding of these rheumatological diseases is a must for favorable outcomes in patients.

CATASTROPHIC ANTIPHOSPHOLIPID ANTIBODY SYNDROME(CAPS)

A rare but potentially life-threatening variant of Antiphospholipid antibody syndrome (APS) which is characterized by aggressive microvascular occlusion in multiple organ systems. Less than 1 % of all patients with APS may develop CAPS. Among such patients, 90 % have Primary APS while 10% may have a concomitant rheumatological illness and is called secondary APS. Secondary APS is seen in SLE, Sjögren syndrome, systemic sclerosis, rheumatoid arthritis (RA), lupus-like disease, and a small percentage of ulcerative rectal colitis (URC).

Patients with CAPS have three traits in common- clinical evidence of vaso-occulsion in organ system, elevated levels of antiphospholipid antibodies in circulation and histopathological evidence of thrombosis in multiple small caliber vessels, occasionally in large vessels too. The following criteria has been designed for diagnosis of CAPS (Fig 1) and incidence of organ involvement in CAPS (Fig 2)

Criteria
1. Evidence of involvement of three or more organs, systems, and/or tissues
2. Development of manifestations simultaneously or in less than a week
3. Confirmation by histopathology of small vessel occlusion in at least one organ or tissue
4. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, and/or anti-beta2-glycoprotein I antibodies)
Classification
Definite catastrophic APS
Requires all four criteria
Probable catastrophic APS
All four criteria, except for only two organs, systems, and/or sites of tissue involvement **or**
All four criteria, except for the laboratory confirmation at least six weeks apart due to the early death of a patient never tested for aPL before the catastrophic APS **or**
Criteria 1, 2, and 4 above **or**
1, 3, and 4 and the development of a third event in more than a week but less than a month, despite anticoagulation

Fig1

RENAL	78%
PULMONARY	66%
CNS	56%
CUTANEOUS	50%
GASTROINTESTINAL	38%
HEPATIC	34%
ADRENAL	13%
UROGENITAL	6%

Fig 2

Common triggers for development of this aggressive disease are infections, surgery, malignancy, trauma, pregnancy, oral contraceptives and cessation of warfarin in an APS patient. It may be usually suspected in young female patients with severe systemic involvement, Venereal Disease Research Laboratory (VDRL) (+), thrombocytopenia, pancytopenia, hemolytic anemia. Mortality due to delay in diagnosis or delay in initiation of appropriate treatment is up to 50%.

Renal dysfunction is the most frequent symptom occurring in about 70% patient characterized by 50 % rise in serum creatinine, severe systemic hypertension (>180/100 mm Hg), and/or proteinuria (>500 mg/24 h). 66% may have pulmonary complication such as ARDS and pulmonary embolism. Cerebral symptoms occur in 60% of patients and may present as infarcts, seizures and venous occlusions. Other symptoms maybe myocardial infarction, Livedo reticularis, skin necrosis, hepatic or splenic infarctions.

Treatment has three goals: 1. Control the cytokine storm with intravenous methylprednisolone pulse 1gm/day for three days and maintenance oral dose of 1-2mg/kg body weight in divided doses then on. 2, Treat and prevent further thrombosis using Unfractionated heparin. A 5000 U bolus of heparin, followed by a continuous infusion of 1500 U/h with aPTT monitoring should be done at first suspicion on CAPS. When the clinical course of the disease is satisfactory and the patient tolerates oral administration, coumarine agents (sodium warfarin) should be started up to an INR >3 and ≤4.5. 3, reduce the burden of circulating autoantibodies with plasmapheresis or intravenous immunoglobulin. Pulse Cyclophosphamide or Rituximab may be used in resistant cases.

PULMONARY RENAL SYNDROME(PRS)

The term “pulmonary-renal syndrome” is characterized by rapidly progressing glomerulonephritis (RPGN) and diffuse alveolar bleeding (DAB) secondary to an autoimmune process. From the immunopathological perspective, three entities have been described: antibody mediated (type 1), immune complex mediated (type 2), and pauci-immune (type 3). Type 1 is related to anti-glomerular basal membrane antibodies (anti-GBM), type 2 is related to SLE, and type 3 to vasculitis associated with neutrophil cytoplasmic antibodies (ANCA)

The most common causes of PRS are vasculitis associated with neutrophil cytoplasmic antibodies (ANCA) in 56–77.5 % of the cases, followed by anti-GBM Ab, representing 12.5–17.5 % of the patients. Some of the less frequent causes (<10 %) are double positive disease (ANCA+MB) APS-associated vasculitis, SLE-associated vasculitis, and IgA vasculitis (Purpura Henoch-Schönlein).

The prevailing antigen in ANCA-associated PRS is myeloperoxidase (MPO) with positive ANCA in 82 %. MPO together with older age and the need for hemodialysis are associated with a shorter survival. As is the case with any autoimmune emergency, there is no time to wait for the immunology results or the results of the renal biopsy and bronchoalveolar lavage. Fig 3-diagnostic workup of PRS

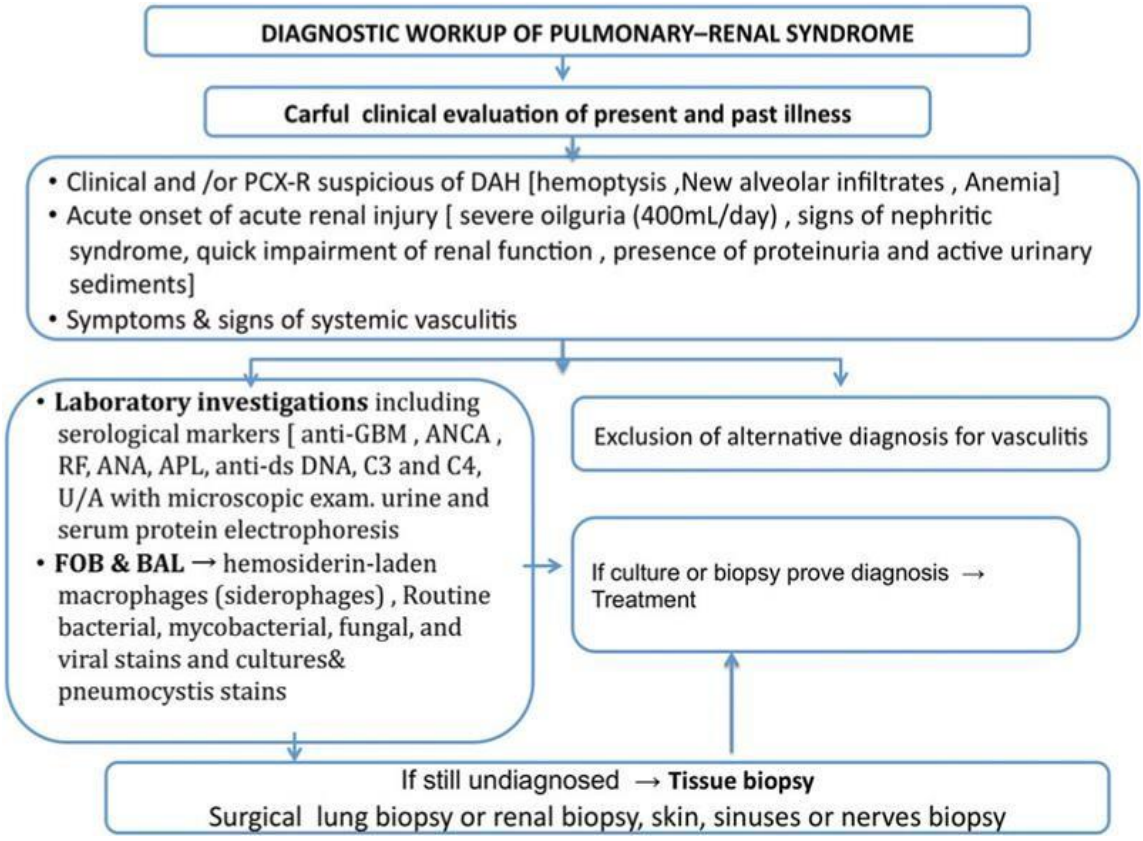

Fig 3

Immediate initiation of methylprednisolone 15–20 mg/day for three to five continuous days give the best results and continues to be the first drug of choice. A maintenance dose of 1–2 mg/kg/dose with concomitant use of Cyclophosphamide 0.4-0.6g/m2 is advised. Plasmapheresis and anti-CD20 rituximab have also demonstrated positive outcomes.

ATLANTO-OCCIPITAL JOINT INSTABILITY

Cervical joint erosion in patients with long standing RA leads to vertebral malalignment, including subluxation, which causes pain, neurologic deficits, and deformity. The upper cervical spine is usually affected, which is manifested by the instability between C1 and C2 vertebrae (atlanto-axial subluxation – AAS) occurring in about 65% of patients.

Anterior subluxation occurs most frequently (75% of all AAS) while posterior and lateral are less frequent. Cervical spine involvement can manifest as the pain in the neck, nape of the neck and head. In advanced cases they may lead to neurological defects in the form of sensory disturbances, muscle weakness and even to death.

A neurological examination may be difficult and sometimes unrewarding due to severe joint deformities, muscle wasting, and entrapment neuropathies secondary to RA. Sensory disturbances in the extremities indicate a spinal cord lesion. It may be unwise to passively flex cervical spine maximally in RA patients, as C1–C2 subluxation may be initially clinically silent.

Radiographs with dynamic views in flexion and extension showing > 3 mm between C1 and dens (increased anterior atlantodental interval-AADI) indicates atlanto-occipital subluxation. Greater the AADI, greater the chances of spinal compression. An AADI>8 mm is an indication for surgical stabilization. Magnetic resonance imaging is a method of choice for the assessment of cervical spine in patients with RA. It precisely assesses the location of all bone structures, in particular the location of the odontoid process with regard to foramen magnum. It allows for the detection of inflammatory lesions in the joints: inflammation of the synovial membrane and the creation of pannus. It is also the best method for the detection of spinal cord compression. Therefore, early diagnosis of AAI may be possible.

MACROPHAGE ACTIVATION SYNDROME (MAS)

MAS is a life-threatening complication of rheumatic diseases, requiring immediate and appropriate treatment. It is caused by an imbalance of the immune system, leading to uninterrupted hyperstimulation of the immune cells.

The most common autoimmune diseases associated with MAS are systemic juvenile idiopathic arthritis (SJIA), followed by systemic lupus erythematosus (SLE), Kawasaki disease (KD), and juvenile dermatomyositis (JDM). The symptoms of MAS are quite similar to those of many active autoimmune diseases or severe sepsis; therefore, it is quite difficult to make a diagnosis.

The classical signs and symptoms of patients with MAS are a persistent high-grade fever, hepatosplenomegaly, lymph-adenopathy, and hemorrhagic manifestations. Abnormal results of investigation include cytopenia, coagulopathy, and hyperferritinemia. Diagnostic criteria is summarised in Fig 4

Clinical Criteria	Fever (>38°C)
	Hepatomegaly (≥3 cm below the costal arch)
	Splenomegaly (≥3 cm below the costal arch)
	Hemorrhagic manifestations (purpura, easy bruising, or mucosal bleeding)
	Central nervous system dysfunction (irritability, disorientation, lethargy, headache, seizures, or coma)
Laboratory Criteria	2 of 3: white blood cell count ≤4.0×109/L, hemoglobin ≤90 g/L, or platelet ≤150×109/L)
	Aspartate aminotransferase (AST) (>40 units/L)
	Lactate dehydrogenase (LDH) (>567 units/L)
	Fibrinogen ≤1.5 g/L
	Triglycerides >178 mg/dL
	Ferritin >500 µg/L
Diagnosis of MAS if 1 Clinical + 2 Laboratory	
OR	
Histopathologic criteria	Evidence of macrophage hemophagocytosis in the bone marrow aspirate

Fig 4

An early diagnosis and prompt initial treatment are both key factors for a favourable outcome. However, the features of MAS are similar to a disease flare-up and a systemic infection, making an early diagnosis challenging. The mainstay of MAS treatment is glucocorticoid therapy. An intravenous methylprednisolone 30 mg/kg/dose (maximum 1 g) for 1–3 days is initiated. If the patients respond well to this it is decreased to 2–3 mg/kg/day in a divided dose. For the nonresponders, an additional therapy with cyclosporin A 2–7

mg/kg/day is recommended. For patients who are refractory to both steroids and cyclosporin, other agents may be considered (Fig 5)

Summary of treatment for macrophage activation syndrome

Drugs	Doses
First choice-treatment	
Methylprednisolone	30 mg/kg/day (for 3-5 days)
Cyclosporine A	3-7 mg/kg/day
Other treatment strategies	
High-dose intravenous immunoglobulins	400 mg/kg/day (for 5 days)
Antithymocyte globulins	10 mg/kg/day (for 5 days)
Etanercept	0.4 mg/kg/dose (twice weekly)

Fig 5

In summary, a thorough understanding of the rheumatological illnesses and anticipation of such emergencies in the course of disease can aid in early diagnosis and prompt treatment of these life threatening conditions.

JOURNAL SCAN

Section Editors

Dr Chakrapani M

Dr B.Sadananda Naik

Summaries of important published articles

SGLT2 inhibitors scored over other OHAs in diabetic patients with NAFLD Jang H, Kim Y, Lee DH, et al. Outcomes of Various Classes of Oral Antidiabetic Drugs on Nonalcoholic Fatty Liver Disease. *JAMA Intern Med.* Published online February 12, 2024. doi:10.1001/jamainternmed.2023.8029

In this Korean study involving 80 178 patients with diabetes mellitus and NAFLD [Non Alcoholic Fatty Liver Disease] where the patients were treated with sulfonylureas, SGLT2 inhibitors, thiazolidinediones and DPP-4 inhibitors. The study concluded that SGLT2 inhibitors were associated with a higher likelihood of NAFLD regression and lower incidence of adverse liver-related outcome parameters when compared with other OADs.

Sudarshan Kriya Yoga Breathing and a Meditation Program is useful for Physician Burnout Korkmaz A, Bernhardsen GP, Cirit B, Koprucu Suzer G, Kayan H, Biçmen H, Tahra M, Suner A, Lehto SM, Sag D, Saatcioglu F. Sudarshan Kriya Yoga Breathing and a Meditation Program for Burnout Among Physicians: A Randomized Clinical Trial. JAMA Netw Open. 2024 Jan 2;7(1):e2353978. doi: 10.1001/jamanetworkopen.2023.53978.

This is a randomized clinical trial assessed the potential efficacy of SKY[Sudarshan Kriya Yoga] conducted online to determine whether SKY can reduce psychological distress and improve wellness in physicians. The trial assessed the potential efficacy of SKY compared with a stress management education (SME) training as control. In the study which included 129 participants, it was found that the physicians who regularly practiced SKY throughout a 2-month period experienced improvements in wellness and decreased burnout. These data suggest that SKY may be an effective, practical, and safe strategy to increase wellness and mitigate burnout in physicians.

New hope for the victims of venomous snake bite

https://www.science.org/content/article/powerful-new-antivenom-raises-hopes-universal-solution-lethal-snakebites

Synthetic antibody neutralizes a key neurotoxin in different snakes from Asia and Africa

A new synthetic human antibody can neutralize venom from the notorious black mamba and three other snakes.Matthijs Kuijpers/Alamy

Researchers have discovered a potent antibody that can neutralize a key type of neurotoxin produced by four different deadly snake species from South Asia, Southeast Asia, and Africa—a step toward an antivenom that could be used on any of the 200 or so dangerous venomous snakes throughout the world. A paper describing the antibody has been published in *Science Translational Medicine*.

AUTHOR INSTRUCTIONS

GUIDANCE FOR AUTHORS AND CONTRIBUTORS

API DK LAHARI is a quarterly published e magazine of API D. K. CHAPTER , released in the www.apidk.org website with archival options of all the issues released stored in pdf format (each issue) also with download option .The magazine will include academic and non academic articles .The languages included will be English and kannada.We are hopeful that this will give a unique opportunity to all API members to share their vision and views on various aspects of our profession and beyond.

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Instructions on preparation of the manuscript to be submitted

1. Manuscript may be in English/Kannada.
2. Font size -12 (Times New Roman) , double spacing , 1.5 inches margins all around the page.
3. All the write ups should include a Title page with author information
4. Title Page should contain the following : Full name/names of all the authors with contact address, cell number, email id, designation, position in the Institution and a passport sized recent photo

Paper/write up categories

1. Scientific articles
2. Member's accomplishments
3. Obituaries
4. News and Views
5. Residents corner
6. View point
7. Medico legal pearls
8. Journal Watch
9. Patient page
10. Listen to legend
11. Life beyond medicine [Non-medical topics]
12. General health articles [more for lay public]

Scientific articles

1. Case reports

Word count- 1500, Maximum of 03 tables & or figs, 07 Refs

2. Review article

Word count- 3500, Maximum of 5 tables or figs

3. Academic challenge

An interesting case presentation with detailed academic discussion

Abstract, word count -3500, Maximum of 5 tables or figs

4. Diagnostic test and interpretation

Word count- 1500

5. Images in Medicine

Photos with good resolution and quality, Word count -500

Abstract is required for case report, Review article, Academic Challenge, and Diagnostic test and interpretation. Word count is inclusive of abstract.

References should be in Vancouver style.

Member's accomplishments

Brief information by self or others on the accomplishments of our API members in profession, public life, academics and other walks of life

Word count- 1000

Obituaries

Condolence message and short write up on the deceased member, One message -500 words

News and Views

Write up on medical happenings with a personal opinion expressed

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