SLE – Q and A

Q1. Can you explain the cut off value for ANA titres in SLE diagnosis?

The ANA titre is suggested to be at least 1:80 from the EULAR/ACR 2019 guidelines as an entry criterion. It is an arbitrary number based on the fact that most healthy people without SLE won't have a titre of this value (but there will be a few). A positive ANA by itself is not specific enough to diagnose (or classify) a patient with SLE, hence the need for other laboratory tests.

Q2. Is there any significance of how high the titre is fords dna and can it be elevated even with other conditions other than SLE?

Yes, the higher the titre of DNA antibodies, the more significant the finding. It can be used to follow the clinical course with treatment and I have found it useful in many of my patients with SLE. It is quite specific to SLE. Occasionally I have some patients with mixed connective tissue disease (with some overlap features of SLE) also having raised DNA antibodies but one could argue that it in the spectrum of a connective tissue disorder (which is what SLE is part of).

Q3. What is the difference between ENA and DNA antibodies?

An ENA antibody refers to the specific target of the antibody (ie a ribonucleoprotein, RNP). DNA antibodies are a broad term and can include chromatin antibodies. They are different entities. One can have an ENA antibody with DNA antibody, an ENA antibody alone or DNA antibody alone (along with a positive ANA) in a patient wth SLE.

Q4. Can you please explain what discoid lupus means?

Discoid lupus refers to a purple/red disc like lesions on the skin, which can be raised or flat on the skin surface, commonly affecting the scalp, face or skin in other areas. A skin biopsy can show characteristic immunoglobulin staining at the dermo-epidermal junction.

Q5. Can SLE patient have negative ANA test with immune deficiency?
Answered via talk but would be very unusual unless the person was immune deficient due to the SLE manifestation (ie lupus nephritis leading to loss of IgG in the urine). The commonest immune deficiency in SLE is complement deficiency but it should not be associated with a negative ANA.

Q6. Can you explain the cut off value for ANA titers in SLE diagnosis?
See above

Q7. Can you also give plaquenil as a steroid sparing agent if skin and joint manifestations are not that prominent?

I typically give the drug even if there isn't prominent joint and skin manifestations given its favourable side effect profile but discuss it with each patient as some patients don't like

taking extra tablets and there are potential side effects of Plaquenil (ie retinal toxicity if taken for too long or at high dose). There's evidence, for example, that Plaquenil can reduce the incidence of congenital heart block in patients who may also have SS-A and SS-B antibodies and so may be a good choice in young women of child bearing age with these autoantibodies as well. Always discuss with the patient is my advice.

Q8. Can you please explain what discoid lupus means?
See above

Q9. Why in Complement mediated MCGN is it an activation of the alternate pathway rather than the classical pathway?
The classical pathway is more important in SLE pathogenesis, as shown by genetic disorders that increase the risk of SLE in those with, say, inherited deletions of C4. Also, patients with autoantibodies to C1q are found in much higher numbers in SLE patients than in healthy controls.

Q10. Is antiphospholipid syndrome diagnosed solely based on antibodies? Or do you need clinical features too?
The syndrome is diagnosed on the basis of pregnancy complications (recurrent early miscarriages or a late miscarriage etc) or venous/arterial thrombosis in the setting of at least of a positive antiphospholipid antibody test that has been repeated at least 12 weeks apart.

Q11. For SLE, after HCQ and steroids is the next step AZA/MTX or MMF?
It depends on the manifestation of SLE. If there is renal/neuro or another severe manifestations, one may choose cyclophosphamide but alternatives would be MMF/AZA or methotrexate depending on the severity. If milder, it depends on the dose of steroids that controls symptoms/signs. If one can control the symptoms with <7.5 mg/day, one may just stick with steroids but often a steroid sparing agent is required.

Q12. If lupus nephritis is the only criteria fulfilled, which types can be diagnosed confidently based on histology alone?
You can diagnose any of the lupus nephritis classes with a combination of direct immunofluorescence (DIF) and histopathology and EM. I don't believe you could diagnose Lupus nephritis without having the DIF as part of the strategy.

Q13. Which classes of lupus nephritis do you treat - is it only class 3 & 4?
We typically initiate treatment for Lupus nephritis Class 3 or 4 but there are some experts who also treat Class V (membranous) but there is no consensus regarding Class V and it would depend on the nephrologist, degree of proteinuria and renal biopsy findings.

Q14. For lupus nephritis can you treat them with hydroxychloroquine for maintenance or should it be azathioprine/mycophenolate
Hydroxychloroquine is not considered strong immune suppression and would be inadequate as a maintenance strategy alone for Lupus nephritis. Using Imuran or MMF would be a reasonable strategy of maintaining remission.

Q15. Can you please elaborate a little based on this mcq?
serum markers affected by treatment?lupus anticoagulation /anticardiolipin /anti beta 2 glycoprotein antibody? ans B? clarification please ? //prothrombin gene mutation ?

The question doesn't make a lot of sense (sometimes remembered questions miss a key part of the stem). Serum markers of lupus affected by treatment? None of the answers would be correct. Or do you mean in APS?

HUS/TTP – Q and A

Q1. Is shiga toxin HUS related to adamsT13 at all?

No

Q2. Does plasma exchange remove complement (i.e why do we not use for complement mediated TMA

In plasma exchange you will remove everything including some of the complements too. But eculizumab will prevent ongoing complement activity. Remember complement proteins are relentlessly produced in the body- primarily the liver.

MCQs on Vasculitis, TMA, TTP ans HUS – Q and A

Q1. For the last Q is the PR3 +ve a red herring?
Yes it was - MPA can be either MPO or PR3 positive. And as we discussed the antibody type matters due to differences in prognosis. Therefore the way to present cases in clinic are the phenotype followed by the serotype, eg in this case MPA with PR3
(in the actual presentation I gave an MPO antibody so as not to cause this confusion - apologies)

Q2. Does PLEX do any harm if CM-HUS and diagnostic uncertainty early on?
(i.e. Question 2 suspect CM-HUS, but PLASMIC score could be TTP, so would you start with PLEX?
PLEX does not cause additional harm (as discussed there is risk during line insertion, and fever with plasma), and in fact can normalise the LDH / platelets / Hb in CMHUS (but is less likely to improve the patient's renal function)
Therefore the workflow - if there's any doubt - will be PLEX, and await ADAMTS13 to differentiate the diseases.

Q3. Past Q:39 f with wt loss and myalgia, +ve rash on exam. +ve MPO and PR3 and normal eosinophils,
a- MPA, b GPA, C Churg-Strauss D, Goodpastures and E polyarteritis nodosa
Tricky!

Not EGPA because eos normal
Not PAN because ANCAs are positive
Not Goodpasture's because antiGBM isn't given
Dual PR3/MPO are associated with levamisole as discussed, but unclear of the significance in primary AAV (https://www.longdom.org/open-access/clinical-outcomes-of-patients-with-dual-positivity-for-proteinase-3-andmyeloperoxidase-specific-antineutrophil-cytoplasmic-antibodies-2155-9899-1000335.pdf)
The age for GPA (typically 45-65yo) is younger than MPA (55-75yo) (https://www.nature.com/articles/s41572-020-0204-y)
So....?GPA
But I think the answer is really unclear

Q4. For the MCQ question on MPA, the question states it is PR3 ANCA positive. Isn't MPA more likely assoc with MPO?
Yes true it was a bit of a red herring - MPA can be either MPO or PR3 positive. And as we discussed the antibody type matters due to differences in prognosis
Therefore, the way to present cases in clinic are the phenotype followed by the serotype eg in this case MPA with PR3
(in the actual presentation I gave an MPO antibody so as not to cause this confusion - apologies)

Q5. Why is there not benefit of giving antibiotics for ST-HUS?
Controversial. On one hand it's thought that giving antibiotics increase the risk of HUS development due to the production of shiga toxin! In other studies it's been found to decrease the severity and mortality of STEC HUS. There is ongoing work in the areas of vaccination, toxin receptor antibodies, probiotics (https://www.frontiersin.org/articles/10.3389/fcimb.2020.00169/full) in this area but still quite young

Q6. Similar to above. Is not finding granulomas more suggestive for MPA? Despite PR3 being positive?
Yes true it was a bit of a red herring - MPA can be either MPO or PR3 positive. And as we discussed the antibody type matters due to differences in prognosis
Therefore the way to present cases in clinic are the phenotype followed by the serotype eg in this case MPA with PR3
(in the actual presentation I gave an MPO antibody so as not to cause this confusion - apologies)

Q7. For the last question, is the reason GPA was ruled out because of the absence of granulomas?
Yes true it was a bit of a red herring - MPA can be either MPO or PR3 positive. And as we discussed the antibody type matters due to differences in prognosis
Therefore the way to present cases in clinic are the phenotype followed by the serotype eg in this case MPA with PR3
(in the actual presentation I gave an MPO antibody so as not to cause this confusion - apologies)

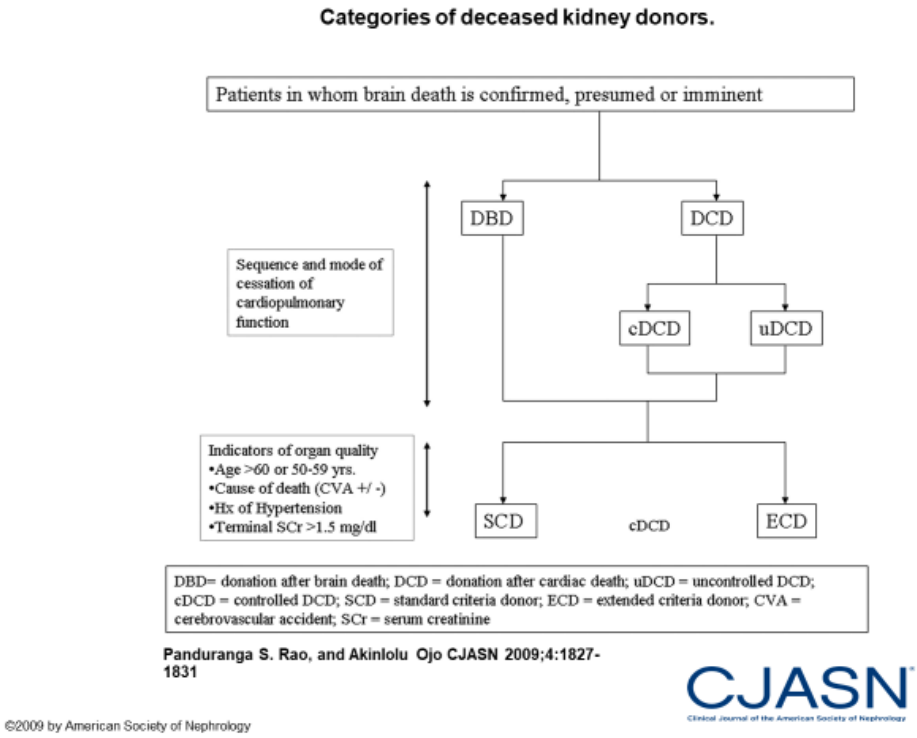
Renal Transplant – Q and A

Q1. Who decides whether a kidney will be accepted or not? Is it the nephrologist or a joint decision?

The Transplant-Nephrologist on Call will make the decision on behalf of the team. Transplant Surgical colleagues may be consulted if there are any potential surgical issues. Sometimes the other members of the team may be consulted.

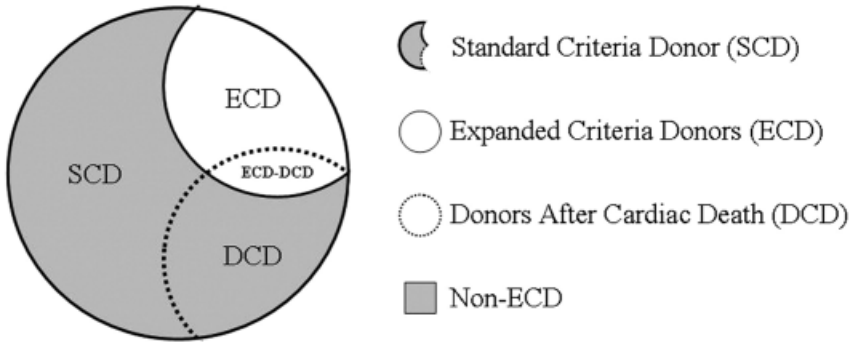
The Tx-Nephrologist replies to the Donor coordinator who makes the offer (usually within 45 min) with Acceptance or Decline. If accepted, he/she informs the Renal Reg on call and the Surgical team.

Q2. Is there any difference in rate of primary non function between DCD and ECD?



I had skipped the slide regarding ECD. ECD, as shown in the slide above, is a donor>60 years or 50-59 years old with one of the following: HTN, Serum Creatinine>120 or CVA as the cause of death.

Categories within the deceased kidney donor pool: SCD, ECD, and DCD.



Note: Not drawn to scale. Source: SRTR.

SRTR

Panduranga S. Rao, and Akinlolu Ojo CJASN 2009;4:1827-1831

CJASN
Clinical Journal of the American Society of Nephrology

DCD donors can also be ECD. That would make the risk of Delayed Graft Function higher. However, the incidence of Primary Non-Function in DCD vs ECD(DBD) has not been studied according to my knowledge.

Q3. Will it be possible to stop immunosuppressives for transplant pt and if yes, when?
Inducing Tolerance is the holy grail of Transplantation, but unlikely in the foreseeable future. Tolerance studies have also used minimal immunosuppression.
If the recipient has serious infection or malignancy (Melanoma..) we may discuss the need to stop immunosuppression and switch back to dialysis.

Q4. Is there any increased risk of CKD in donors when compared to general population?
Recent data support that living donors may experience a small increased risk of severe CKD and ESKD compared with healthy nondonors. For most donors, the 15-year risk of kidney failure is <1%, but for certain populations, such as young, black men, this risk may be higher- Aboriginal donors in Australia.
Risk of ESKD higher than in Non-Donors but lower than in general population.

Ref: Lentine et al., CJASN April 2019

Q5. In pregnancy is the risk of HTN/preeclampsia only with people who have donated or in women with congenital single kidney as well?

Both groups.

Interesting question-please look at the interesting article quoted:

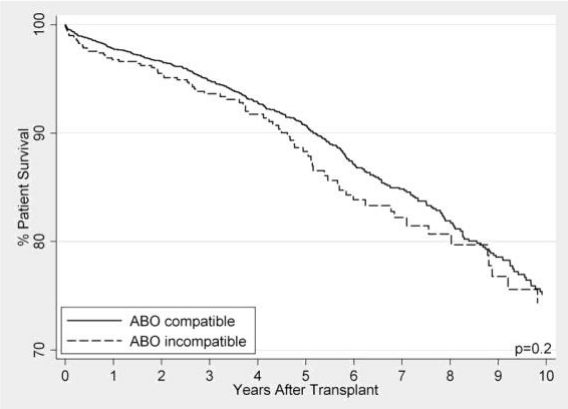
Pregnancy in women known to be living with a single kidney

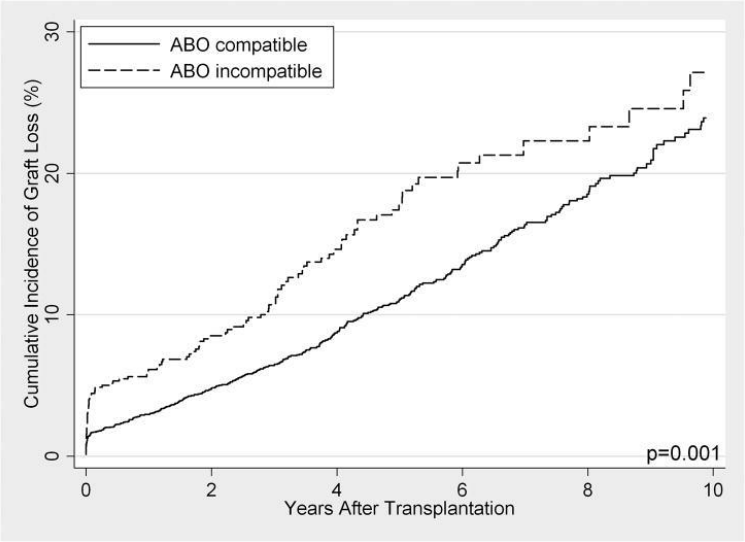
Obstetric Medicine
The Royal Society of Medicine Journals

Steele et al., Obstet Med. 2019 Mar; 12(1): 22–26.

Q6. Young ladies with renal transplant and Mycophenate should be placed on OCP/contraception routinely?
The need for contraception whilst being on Mycophenolate is always discussed with them. The partner could practice contraception as well.

Q7. Is there any long term data on outcomes ABO incompatible transplants as the meta analysis just showed a 1 yr follow up
Montomery et al published in Transplantation journal in 2012: 10 years retrospective registry data: No difference in patient survival but inferior graft survival compared to ABO compatible ones. However, much better than being on dialysis.





Q8.Case scenario in our notes use Everoluimus, whilst in the lecture has Sorilomus? Are they interchangeable? and can you please explain the answer once again, why the change from everolimus to tacrolimus should be considered?

Sorry for the confusion. Studies were done with Sirolimus with the primary intent of reducing the risk of SCCs. Everolimus is more commonly being used now in place of Sirolimus. Especially after the TRANSFORM trial wherein reduced dose CNI+ Everolimus was used. A paper by Ying et al (American Journal of transplantation 2018: 18(12):2977-2986.) performed a secondary analysis of ANZ patients in Transform trial and indicated that the risk of all cancers and SCC of skin was reduced in the Evero+ reduced CNI arm.

Q9. Do low risk patients also receive valgancyclovir CMV prophylaxis but for a shorter period?

Yes: D+/R+ or R+/D- pairs for 3 months generally.

If both are negative D-/R-: we don't use any prophylaxis but keep a close watch.

D+/R- is the high risk group we discussed: 6 months