



SCHOOL OF MEDICINE

DIVISION OF NEPHROLOGY
PRESENTS



Renal Week ISBP 2015

16-19th September 2015

Therapeutic Apheresis Medicine; The Evidence and the Guidelines (ASFA)

Hotel Azimut, St. Petersburg, Russia.

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Saturday Sept 19, 2015 12:30-12:55

Disclosure

Relevant Financial Relationships

None

Relevant Non-Financial Relationships

Serving Board Member, American Society for Apheresis
Member, JCA Special Issue Committee

Slides

Many modified from ASFA, Jeff Winters, Robert Weinstein, Yossi Schwartz

Off Label Usage

None

Outline:

Therapeutic Apheresis Medicine (TAM)

- Historical Evidence base of TAM
- TAM is (neglected) part of clinical nephrology
- Challenges and Barriers to Expanding Knowledge in TAM
- Existing Evidence Base: JCA Special Issue

Apheresis Medicine: Saint Petersburg, Russia

Therapeutic Apheresis and Dialysis 2014; 18(2):117–121

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Review Article

Russian Pioneers of Therapeutic Hemapheresis and Extracorporeal Hemocorrection: 100-Year Anniversary of the World's First Successful Plasmapheresis

Alexey A Sokolov¹ and Andrey G Solovyev²

¹Medical Military Academy, and ²Institute for Experimental Medicine NW RAMS, Saint-Petersburg, Russia

Apheresis Medicine: Saint Petersburg, Russia



FIG. 1. Group of buildings for the Division of Infectious Diseases, Lebedev Street, Saint-Petersburg. (Bacteriological Laboratory was located in the 3rd building). This complex was demolished in 1985.

Extracorporeal Therapies RPA 2001

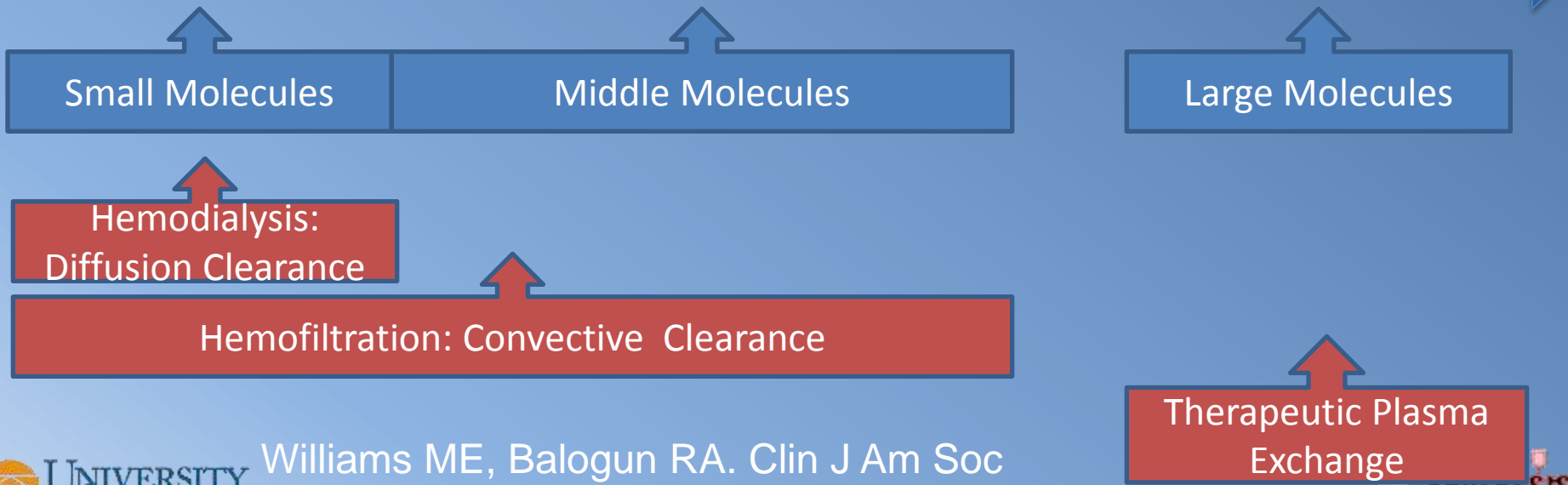
- Hemodialysis
- Hemofiltration
- Hemodiafiltration
- Continuous renal replacement therapies
- Hemoperfusion
- **Apheresis (TPE)**
- Immunoadsorption
- Liver dialysis

Blood Purification; Size Matters

Immunoglobulin G
 160kDa; 2 LC: 23-25 kDa each; 2 HC:~53 kDa each

Molecular Weight kD

BUN	Cr	VitB12	B2-mic	K Lig C	L Lig C	Album	IgG
0.06	0.113	1.355	11.8	25	50	66	160



Williams ME, Balogun RA. Clin J Am Soc Nephrol. 2014 Jan; 9(1):181-90.

Apheresis Technology

- Separation of blood components
- Removal of the selected component
- Re-infusion of the remaining components
- It allows for processing large volumes of blood to collect or exchange different types of cells or blood components.

Manual “Plasmapheresis”

PLASMA REMOVAL WITH RETURN OF CORPUSCLES (PLASMAPHAERESIS)

FIRST PAPER

JOHN J. ABEL, L. G. ROWNTREE AND B. B. TURNER

From the Pharmacological Laboratory of the Johns Hopkins University

Received for publication, July 16, 1914

I. In connection with our experiments on vividiffusion with a view to the ultimate use of the method for the relief of toxæmia the idea suggested itself to try the effects of the repeated removal of considerable quantities of blood, replacing the plasma by Locke's solution and reinjecting this together with the sedimented corpuscles.

J. Pharmacol Exp Ther, 5:625, 1914

J Clin Apher. 2010 00;25(5):240-249.
Okafor C, Ward DM Balogun RA.

Russkiy Vrach (Russian Physician) Journal Cover Vol. XIII, no. 18, 1914 (page. 637)

Русский Врачъ.

8509

ЕЖЕНЕДЕЛЬНЫЙ ЖУРНАЛЪ,

посвященный всемъ отраслямъ клинической медицины, общественной и частной гигиенѣ и вопросамъ врачебнаго быта.

Органъ, основанный въ память В. А. МАНАССЕЙНА.

Подъ редакціей д-ра С. В. ВЛАДИСЛАВЛЕВА.

ТОМЪ XIII.

(№№ 1—52, стр. 1—1628).

ПЕТРОГРАДЪ.
ИЗДАНИЕ О. А. РИККЕРЪ.
1914 г.

Русский Врачъ, 1914, № 18. В. А. Юревичъ и Н. К. Розенбергъ: О промывании крови внѣ организма. 637

хроматина ядромъ. Содержавшія включения ядотки мѣстами располагались цѣлыми группами и находились близко другъ къ другу. Въ тѣхъ участкахъ опухоли, гдѣ омертвѣвшихъ клетокъ не находилось, большая клетка была, но онѣ не содержали включений.

Откуда происходятъ большія клетки? По мнѣнію, высказанному *Robley* (1907), онѣ происходятъ изъ эндотелия лимфатическихъ сосудовъ. И въ описанной опухоли встрѣчались участки, гдѣ ясно была видна связь такихъ клетокъ съ эндотелиемъ лимфатическихъ сосудовъ. Что касается включений въ большія клетки, то это не были ли плазматическія, или оторвавшіяся клетки, или безцѣпныя кровяныя тѣла, или эозинофилы, або, какъ это было обнаружено различными окрашиваниями, такія клетки въ опухоли не было вовсе. Такимъ образомъ эти включения представляли собой отщепенія опухолевыхъ клетокъ и распады ихъ, а затѣвавшія ихъ большія эндотелиальныя клетки можно считать фагоцитами.

Какую-же роль играютъ эти фагоциты въ опухоли? Принимая во вниманіе, что въ тѣхъ участкахъ опухоли, гдѣ клетки не сохранили признаковъ живучести, фагоцитоза не наблюдается и эндотелиальныя клетки, повидному, питаются доходящими до нихъ питательными соками, а фагоцитозъ виденъ въ тѣхъ мѣстахъ, гдѣ находятся омертвѣвшія клетки, при чемъ даже приходится различать фагоцитозъ, можно предполагать, что фагоциты обнаруживаютъ анатомическое отношеніе къ омертвѣвшимъ клеткамъ, способствуютъ росту опухоли тѣмъ, что уничтожаютъ отщепенія клетокъ и ихъ распадающія части, давая больше простора для жизни и размноженія опухолевыхъ клетокъ.

XIII. Изъ бактериологической лабораторіи при кафедрѣ заразныхъ болезней въ В. Медицинской Академіи.

Въ вопросу о промываніи крови внѣ организма и о низинной стойкости красныхъ кровяныхъ шариковъ.

Вспомогательное изслѣдованіе.

Проф. В. А. Юревича и д-ра Н. К. Розенберга.

Цѣль, поставленная нами себѣ, заключалась въ осуществленіи идеи возможно болѣе энергичнаго промыванія организма въ случаяхъ тяжелыхъ отравленій различнаго происхожденія и, слѣдя, въ случаѣхъ необходимости быстрого освобожденія организма отъ накопившихся въ немъ въ чрезвычайномъ количествѣ токсическихъ веществъ. Идея промыванія широко проводится въ настоящее время, но исключительно въ видѣ обильнаго вливанія введенія въ организмъ тѣмъ или другимъ путемъ

физиологическаго раствора поваренной соли, въ конечномъ разсчетѣ на выведеніе токсическихъ веществъ естественными путями. Однако такое промываніе оказывается или недостаточнымъ, или вовсе неэффективнымъ, когда дѣятельность почекъ резко нарушена; типичнымъ приборомъ могутъ служить случаи почечекривы.

Освобожденіе крови отъ части ядовитыхъ веществъ, перегрузившихъ организмъ, возможно либо, какъ это дѣлается иной разъ и теперь, простымъ кровопусканіемъ, понижаящимъ въ то-же время и кровяное давленіе, либо болѣе сложными способами. Первая мысль, которая несомнѣно напрашивается въ разрѣшеніи этого вопроса, заключается въ томъ, чтобы помочь почкамъ въ освобожденіи крови отъ ядовитыхъ веществъ, подвигнувъ кровь діализу. 2-ая возможность быстрого частичнаго освобожденія крови отъ вредныхъ продуктовъ состоитъ въ обильномъ кровопусканіи съ послѣдующимъ или одновременнымъ вливаніемъ физиологическаго раствора, въ отмытый форминамъ элементъ вливающейся крови и въ отработку введенія ихъ въ организмъ; форминныя элементы крови могутъ быть при этомъ внѣ организма не только отмыты ерѣдѣнными растворами, но и подвергнуты воздействию тѣмъ или другимъ агентомъ въ случаѣ, если они уже послужили въ организмѣ (примѣръ хлоророломъ и т. д.).

Наша изслѣдованія были направлены въ сторону промыванія крови внѣ организма и возврата отмытой крови. Первое, что предлодано при этомъ рѣшить, было то, возможно-ли вообще животному безъ особаго для него вреда вернуть въ организмъ количественн стмытую кровь, и затѣмъ, если-бы это оказалось возможнымъ, установивъ, сохраняются-ли форминныя элементы крови, особенно красныя шарикн, послѣ грубого на нихъ воздействия различныхъ агентовъ внѣ организма, способностей работать, а, слѣдя, имѣть-ли быть понесенъ животному организму, интереснаго Большое количество крови, возвращеннаго отмытымъ форминамъ съ элементомъ, послѣдняя питатель была сълужающая.

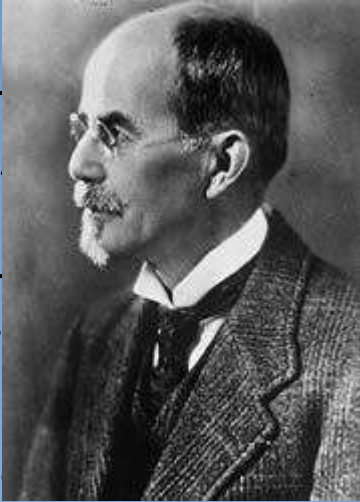
У животныхъ изслѣдованіе былъ введено одинъ изъ способовъ прерыва. Черезъ стѣнныя вѣду, зерны кровянаго и соединенную растворомъ лимонно-кислаго натрія канюлю, установленную черезъ разрывъ въ шкуру, вводились кровь въ извѣстномъ количествѣ въ собранную въ кружку выщербленную прозрачную изолонную емкость лимонно-кислаго натрія. Кровь затѣмъ интродуцировалась, затѣмъ отсасывалась. Въ пробиркѣ вводился физиологическій растворъ поваренной соли, въ которомъ форминныя элементы крови были заботливо вымыты. Послѣ 2-го, а иной разъ и 3-го интродуцированія общей объемъ физиологическаго раствора поваренной соли съ форминами элементами крови доходилъ до полутора для дѣлано одна размѣры, и отмыта тѣмъ же образомъ, послѣдняя до 38°—40°С.

Кровь чрезъ ушныя вены вводилась обрѣвно въ организмъ животного. Служаетъ указывать, что недостаткомъ послѣ вливающейся кровью вводилась въ организмъ физиологическаго раствора и, если нужно было, лаванъ инеюротамъ. Первые-же неудачныя опыты показали, что для того, чтобы животн и съ удороженіемъ забрать стмытую кровь, необходимо вливать значительное количество раствора лимонно-кислаго натрія. Такъ какъ въ нашемъ распоряженіи была центрифуга только съ пробирками вмѣстѣ емкостью въ 45 и 57 см. въ обннн онѣ вливались 20-ая к. см. растворомъ лимонно-кислаго натрія, кровь же забиралась до объема объема въ 45 и 57 см. Этотъ опытъ привелъ къ выводу, что 1,5%-ный растворъ лимонно-кислаго натрія. Особо ошлплого разведенія такимъ растворомъ при обильномъ кровопусканіи требуютъ извѣстныя порціи пшутельной крови. Вотъ почему ошлпды прерыва интродуцированія и извлеченіемъ изъ нее нѣкоторой части ороиздана тѣмъ же растворомъ лимонно-кислаго натрія. При этомъ удалось сбираться кровь не омертвѣвшая до того времени съ промываніемъ и забирающаяся отмытымъ болѣе грубымъ осмомомъ, слѣдя, и была особой чистоты вынѣтъ ядомъ. Оставался одинъ открытій вопросъ, насколько ошлпды въ этомъ послѣднемъ отношеніи: обшлпды съ небольшой кучей при центрифугированіи форминныя элементы крови? Рѣшъ этотъ вопросъ ошлпды была проведена съ центрифугированіемъ крови до полного обшлпды въ тѣхъ случаяхъ, форминамъ 2-хъ к. см. пшутельной или красныхъ шариковъ и затѣмъ въ безцѣпныхъ тѣлахъ и пшутельныхъ. Красныя шарикн при этомъ обшлпды въ лучшъ имѣ, а въ безцѣпныхъ тѣлахъ образуется лопъ

*) Geschwulstsch.: Boon, 1901 г.

Back to the Future: Dialysis & 'Plasmapheresis' historically linked

- Abel J.J., Rowntree L.G., Turner B.B. On the removal of plasma from the circulating blood by means of a dialyzer // Trans. Am. Soc. Pharm. – 1913. – Vol.28. – P.51.
- Abel J.J., Rowntree L.G., Turner B.B. On the removal of plasma from the circulating blood living animals // J. Pharmacol. Exp. Ther. – 1913-1914. – Vol.5 – P.625.
- Abel J.J., Rowntree L.G., Turner B.B. Some considerations on the removal of plasma from the blood // J. Pharmacol. Exp. Ther. – 1913 – 1914. – Vol.5 – P.625.
- Abel J.J., Rowntree L.G., Turner B.B. Plasma removal with return of corpuscles (plasmapheresis) // J. Pharmacol. Exp. Ther. – 1913 – 1914. – Vol.5 – P.625.
- Yurevich V.A., Rozenberg N.K. A question of cleansing blood outside of an organism and the vital stability of red blood cells// Russian Doctor. – 1914. – Vol.13, №18. – P. 637 – 639.

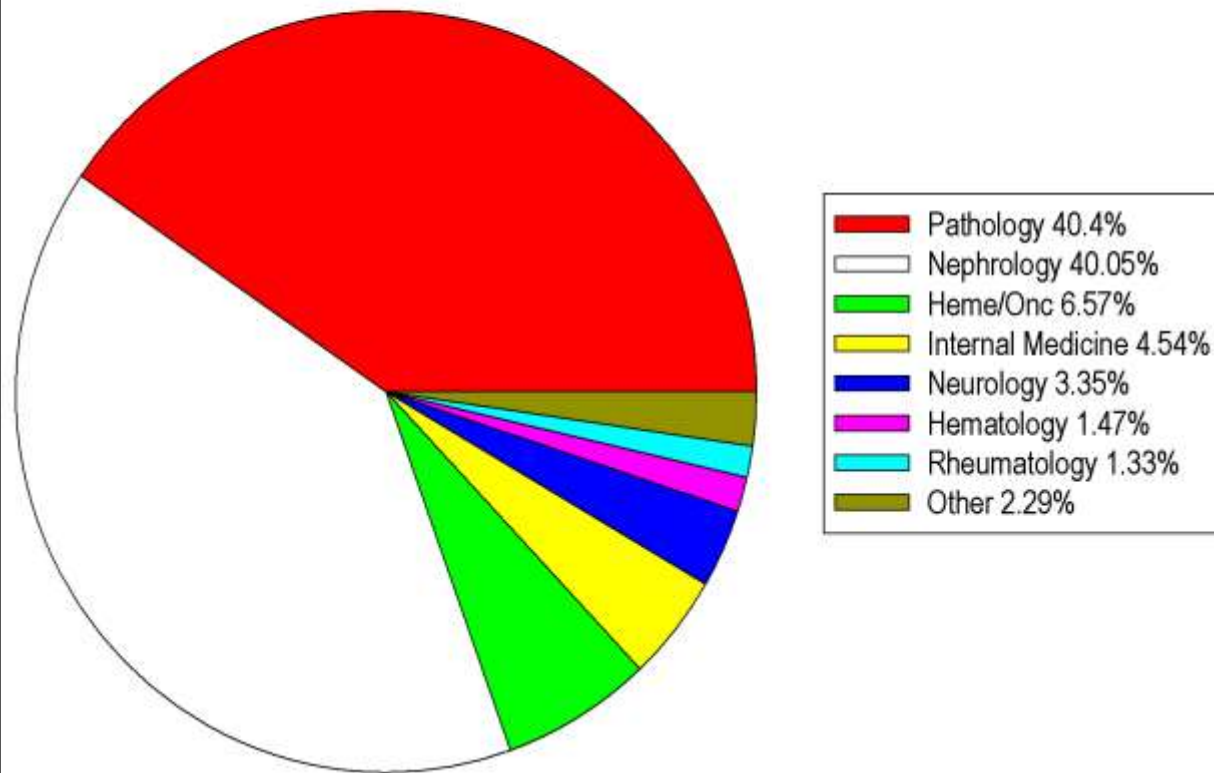


Barriers: Known and Imagined

- Multidisciplinary: child of many parents
- Expensive clinical trials
- “Sham” Procedures: a no no
- End points (and surrogates): not always clear
- Biomarkers: not available for many
- Injudicious, non-evidence based use
- Non-standard/No measure of quality (CAP FACT)
- Physiology/Pathology is not static

Therapeutic Apheresis: Why should I care?

Specialties Performing CPT 36514:
2007 Medicare Claims Data



Family Practice
Pediatric Medicine
Medical Oncology
Anesthesiology
Nurse Practitioners
Orthopedic Surgery
Emergency Medicine
Infectious Disease
Physicians Assistant
Gastroenterology
Pain Management
General Surgery
Urology
Pulmonary Disease
Cardiology
Diagnostic Radiology
Allergy/Immunology
Critical Care
Multispecialty Group
Endocrinology
General Practice

Contributions American Society for Apheresis

- Publication of standards for:
 - Documenting apheresis procedures
 - Qualifications of allied health staff performing apheresis procedures
 - Qualifications for physicians overseeing apheresis procedures
- Development of apheresis requirements for the CAP Laboratory Accreditation Program
- Advocacy for apheresis patients and practitioners
 - Clarification of CMS coverage guidelines
 - Review of insurance company coverage policies
- Publication of evidence-based guidelines for the use of apheresis in clinical practice - five editions
 - Sixth edition is in preparation

What is the Special Edition of the *Journal of Clinical Apheresis*?

- *Journal of Clinical Apheresis*
 - Presents work in all aspects of basic and clinical research, practical applications, emerging technologies and regulation in apheresis and related fields including hematology, nephrology, neurology, rheumatology, transplantation, cellular therapies, blood banking, transfusion medicine and others.
 - Impact factor of 1.933
- Special edition is published every three to seven years
 - Seeks to provide a comprehensive review of the literature of the use of apheresis to treat disease
 - Seeks to objectively evaluate the science supporting or refuting the use of apheresis to treat disease
 - Seeks to provide practical recommendations

Why was the Special Issue of the *Journal of Clinical Apheresis* created?

- Dearth of randomized controlled trials of the use of apheresis
- Between 1976 and 1999*:
 - 592 published articles on the use of apheresis
 - 85 published randomized controlled trials
- Quality of apheresis literature is limited
 - For some diseases ONLY case studies or small series
- Need for evidence-based guidance

*Shehata N, Kouroukis C, Kelton JG. A review of randomized controlled trials using therapeutic apheresis. *Transfus Med Rev* 2002;16:200-229.

Barriers: Known and Imagined

- Multidisciplinary: child of many parents
- Expensive, clinical trials
- “Sham” Procedures: no no
- Injudicious, non-evidence based use
- Non-standard/ No measure of quality (CAP, FACT....)
- Physiology/Pathology is not static

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 - Seeks to objectively evaluate the science supporting or refuting the use of apheresis to treat disease
 - Seeks to provide practical recommendations

History of the Special Edition of the *Journal of Clinical Apheresis*



- 1986 - Edited by Dr. Harvey Klein
- 1993 – Edited by Dr. Ron Strauss
- 2000 – Edited by Dr. Bruce McLeod
 - ASFA Categories first introduced
 - 53 clinical indications categorized

Special Edition of the *Journal of Clinical Apheresis*

- **2007 – Edited by Dr. Zbigniew Szczepiorkowski**
 - Fact sheet format introduced
 - Strength of evidence for the use of apheresis provided
 - 72 clinical indications categorized
- **2010 – Edited by Drs. Beth Shaz and Zbigniew Szczepiorkowski**
 - Category III definition revised
 - Recommendation grades for the use of apheresis provided
- **2013 – Edited by Drs. Beth Shaz and Yossi Schwartz**
 - 78 Clinical indications



Guidelines on the Use of Therapeutic Apheresis in Clinical Practice- Evidence-Based Approach

J Schwarz, Z Szczepiorkowski, M Delaney, J Winters, M Linenberger, Y Wu, R Balogun, A Padmanabhan, M Williams, BH Shaz

Committee consisted of 10 members from diverse fields (membership determined through

published literature reviewed by primary author, who drafted a 'fact sheet' qualifying the literature

incidence, description, management of disease; rationale, technical notes, volume treated, replacement fluid, treatment frequency and duration for T A & references

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2013 Fact Sheet Structure

ANCA-ASSOCIATED RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN)

Incidence: 0.85 per 100,000/year	Procedure TPE TPE TPE	Rec
# of reports RCT R (296)	Articles CT (126)	CR 27 (347)
Type of evidence		

**a presentation.

Description of the disease

ANCA-associated rapidly progressive glomerulonephritis is one cause of the histopathologic entity, rapidly progressive glomerulonephritis (RPGN). RPGN consists of rapid loss of renal function with the histologic finding of crescent formation in over 50% of glomeruli. These crescents represent a proliferation of cells within Bowman's space of the glomerulus due to the accumulation of protein into this space. These cells create a proliferating parietal epithelial cells as well as infiltrating macrophages and monocytes.

RPGN is NOT A SINGLE DISEASE ENTITY but is a clinical syndrome that can result from a number of etiologies. RPGN is divided into three categories based on the immune-deposits pattern in renal biopsy. These categories are:

- 1) Linear deposits of IgG due to autoantibodies to type IV collagen representing anti-glomerular basement membrane disease (anti-GBM). It accounts for 15% of cases. (See fact sheet on anti-glomerular basement antibody disease).
- 2) Granular deposits of immune complexes caused by a variety of GNCs including post-infectious GN, Henoch-Schönlein purpura, IgA nephropathy, membranoproliferative GN, cryoglobulinemia, and IgG4-related disease. Immune-complex RPGN accounts for 50% of cases of RPGN. (See fact sheet on immune-complex RPGN).
- 3) Minimal immune deposits in the glomerulus with the presence of anti-neutrophil antibodies (either C-ANCA or P-ANCA) in the serum. This pattern is called ANCA-associated RPGN, also referred to as ANCA-associated RPGN, is seen in Wegener's granulomatosis (WG) and microscopic polyangiitis (MP) and accounts for 30% of RPGN cases.

It is important for nephrology clinicians to identify the specific category of RPGN present in their patient as TPE treatment protocols and responses differ among the three categories. In this special issue, anti-GBM and immune complex glomerulonephritis, the other major causes of RPGN, are discussed in separate fact sheets.

This fact sheet discusses ONLY ANCA-associated rapidly progressive glomerulonephritis. Pauci-immune GN is characterized by minimal immune deposits in the glomeruli and the presence of anti-neutrophil cytoplasmic antibodies (P-ANCA, C-ANCA) in the serum. ANCA-associated small vessel vasculitis encompasses a clinical spectrum of disease which ranges from small vessel vasculitis to systemic involvement, including microscopic polyangiitis (MP), Wegener's granulomatosis, and the Churg-Strauss syndrome. The presentation of the pulmonary-renal syndrome associated with ANCA is clinically similar to anti-glomerular basement membrane disease (Goodpasture's syndrome). When ANCA and anti-glomerular basement antibodies are both present, the disease should be considered to represent anti-GBM disease. See the fact sheet on anti-glomerular basement antibody disease. Diffuse alveolar hemorrhage (DAH) associated with ANCA vasculitis poses significant risk of mortality.

Current management/treatment

The current standard approach to management of ANCA small vessel vasculitis is immunosuppressive therapy consisting of high-dose corticosteroids and cytotoxic immunosuppressive drugs. TPE has been added to this treatment regimen, such as ANCA with DAH, and also in patients who are dialysis dependent or for whom initiation of dialysis is imminent. Other drugs that have been used include infliximab, rituximab, tumor necrosis factor blockers, calcineurin inhibitors (cyclosporine and tacrolimus), cyclosporin and azathioprine against T cells. The European League Against Rheumatism (EULAR) recommends TPE as an adjunct for selected patients with rapidly progressive renal and/or systemic vessel vasculitis of the kidney.

Rationale for therapeutic apheresis

The presence of ANCA autoantibodies indicates a humoral component to disease pathogenesis and has formed interest in TPE for management. Much of the published experience with TPE includes all forms of RPGN, not just exclusively Wegener's disease or ANCA-associated RPGN, which complicates interpretation of results. Six trials have examined the role of TPE in pauci-immune and immune-complex GN. Of these 3 consisting of a total 87 patients, showed no benefit of TPE over standard therapy. Two trials consisting of 63 patients found benefit in patients who were dialysis dependent at presentation but not those not dialyzed. One trial consisting of 14 patients found benefit in all. These trials suggest that TPE is most beneficial in patients with dialysis dependency (at presentation) and offers no benefit over immunosuppression in nondialyzed disease. A controlled trial of ANCA-associated RPGN of 26 patients suggests TPE may improve prognosis over its non-dialysis dependent patients. A retrospective case series reported effective management of pulmonary hemorrhage in ANCA vasculitis. In a European prospective study of 100 patients presenting with an initial diagnosis of ANCA-associated vasculitis with severe renal involvement, patients received standard therapy of oral corticosteroids and cyclophosphamide and were randomly assigned additional therapy of either TPE or pulse methylprednisolone (1000 mg/d x 3 days). Remission rates in the treatment arm, which included plasma exchange (7 sessions over 14 days) was predictive of dialysis independence at 12 months (54% compared to 29%). In addition, this study required mean Cr >500 mg/dL, <0.5 mg/dL, hemoglobin to remain stable within 40 hours, ANCA positivity, and histologic confirmation to exclude other causes of glomerulonephritis. A subsequent minimal survey of 400 ANCA patients treated with apheresis, however, did not demonstrate efficacy of apheresis in their patient population. A more recent standardized controlled trial (RCT) showed a significant improvement in renal recovery for ANCA patients presenting with Cr >5.8 mg/dL who received TPE compared to pulse methylprednisolone. A randomized international RCT is in progress to establish the efficacy of TPE in addition to immunosuppressive therapy and glucocorticoids in reducing death and end-stage renal disease in ANCA positive vasculitis. (PDXIVAS; ClinicalTrials.gov registration number NCT00867908).

Technical notes

In patients with pulmonary hemorrhage, apheresis with plasma is recommended to avoid fibrinolytic coagulopathy, making true red-plasma replacement.

Volume treated: 1 to 1.5 TPE

Replacement fluid: albumin; plasma when DAH present

Frequency: daily or every other day

Duration and discontinuation/number of procedures

Consider daily procedures in fulminant cases or with pulmonary hemorrhage less containing every 2-3 days for total of 6-9 procedures.

References [93-117]

*As of December 31, 2009 using PubMed and the MeSH search terms ANCA or anti-neutrophil cytoplasmic antibody and glomerulonephritis in glomerular exchange for articles published in the English language. References of the identified articles were searched for additional cases and trials.

ANCA-ASSOCIATED RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (WEGENER'S GRANULOMATOSIS)

Incidence: 0.85 per 100,000/year	Procedure TPE TPE TPE	Recommendation Grade 1A Grade 1C Grade 2C	Category I (dialysis dependence)** I [diffuse alveolar hemorrhage (DAH)] III (dialysis independence)**
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Special Issue, *Clinical application of Therapeutic Apheresis*,
5th edition, *Journal of Clinical Apheresis* 2010;25:83-177

Revision of ASFA Indication Categories V-VI edition (*with examples*)

Category I <u>Likely Grade 1</u> (A, B or C)	First-line therapy: primary stand-alone treatment or in conjunction with other modes of treatment. <i>Acute Guillain-Barré Syndrome; Myasthenia Gravis</i>
Category II <u>Likely Grade 1</u> (A, B or C)	Second-line therapy: stand-alone treatment or in conjunction with other modes of treatment. <i>Acute disseminated encephalomyelitis</i>
Category III <u>Likely Grade 2</u> (A, B or C)	Optimum role of apheresis therapy not established. Decision making should be individualized. <i>TPE for sepsis and multi-organ failure</i>
Category IV <u>Grade 1 or 2</u> (A, B or C)	Published evidence indicates apheresis to be ineffective or harmful. Seek IRB approval. <i>Plasma Exchange for Rheumatoid Arthritis</i>

adapted
from:

Strauss RG et al. J Clin Apher 1993;8:189-94

McLeod BC. J Clin Apher 2000;15:1-5

Szczepiorkowski ZM et al. J Clin Apher 2007;22:96-105

Highlights of the 2013 Special Issue

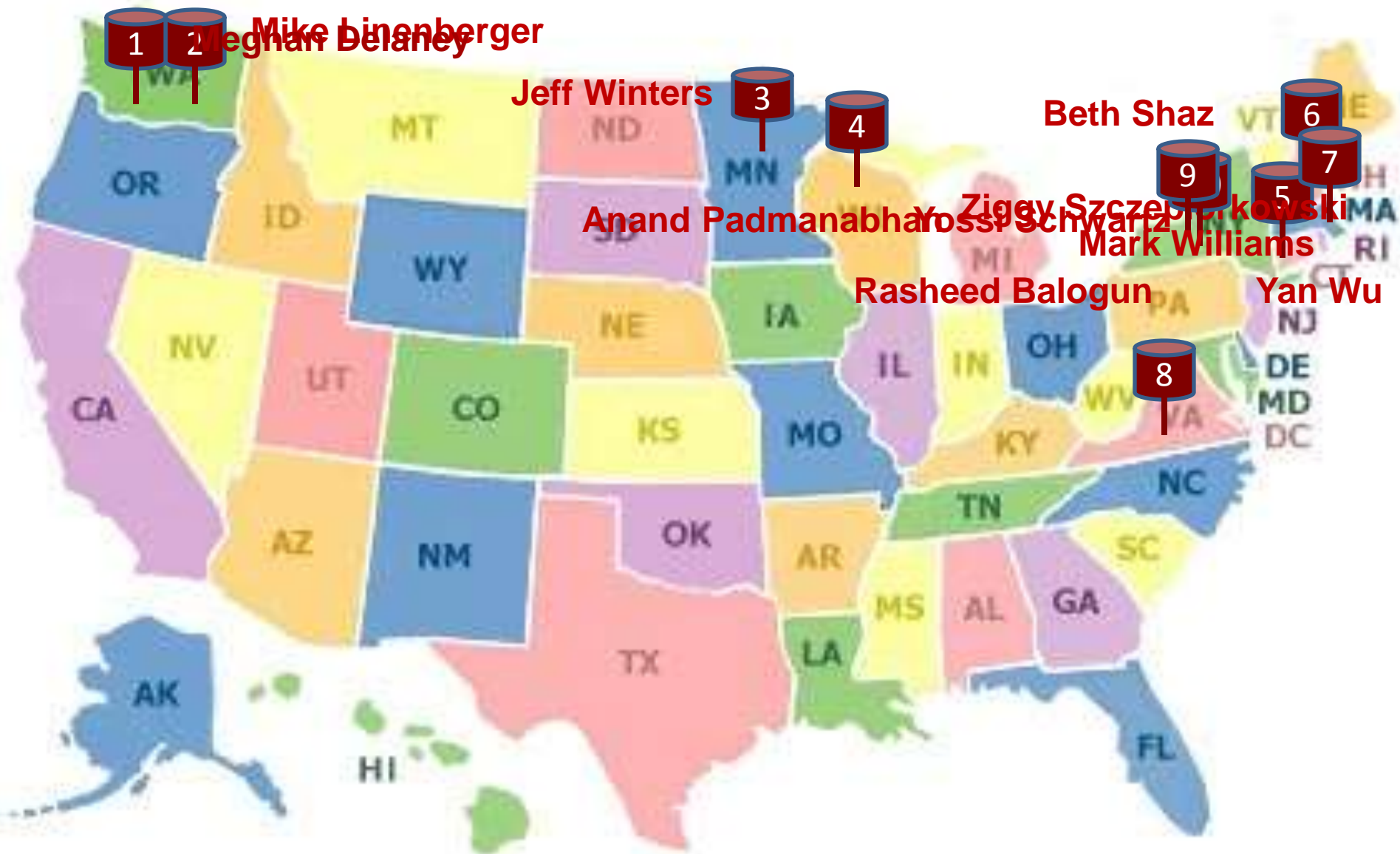
- Compilation of all fact sheets for disease entities which were assigned ASFA categories I, II, III and IV
- **78** diseases/medical conditions are categorized
- In-depth clinical view
 - If apheresis is used in more than one clinical setting in the same disease state, each is treated as a separate indication and is assigned a recommendation grade and category

Example: Solid organ transplantation

- When needed, diseases divided into more than one Fact Sheets,

Example: Sickle Cell Disease acute & non-acute

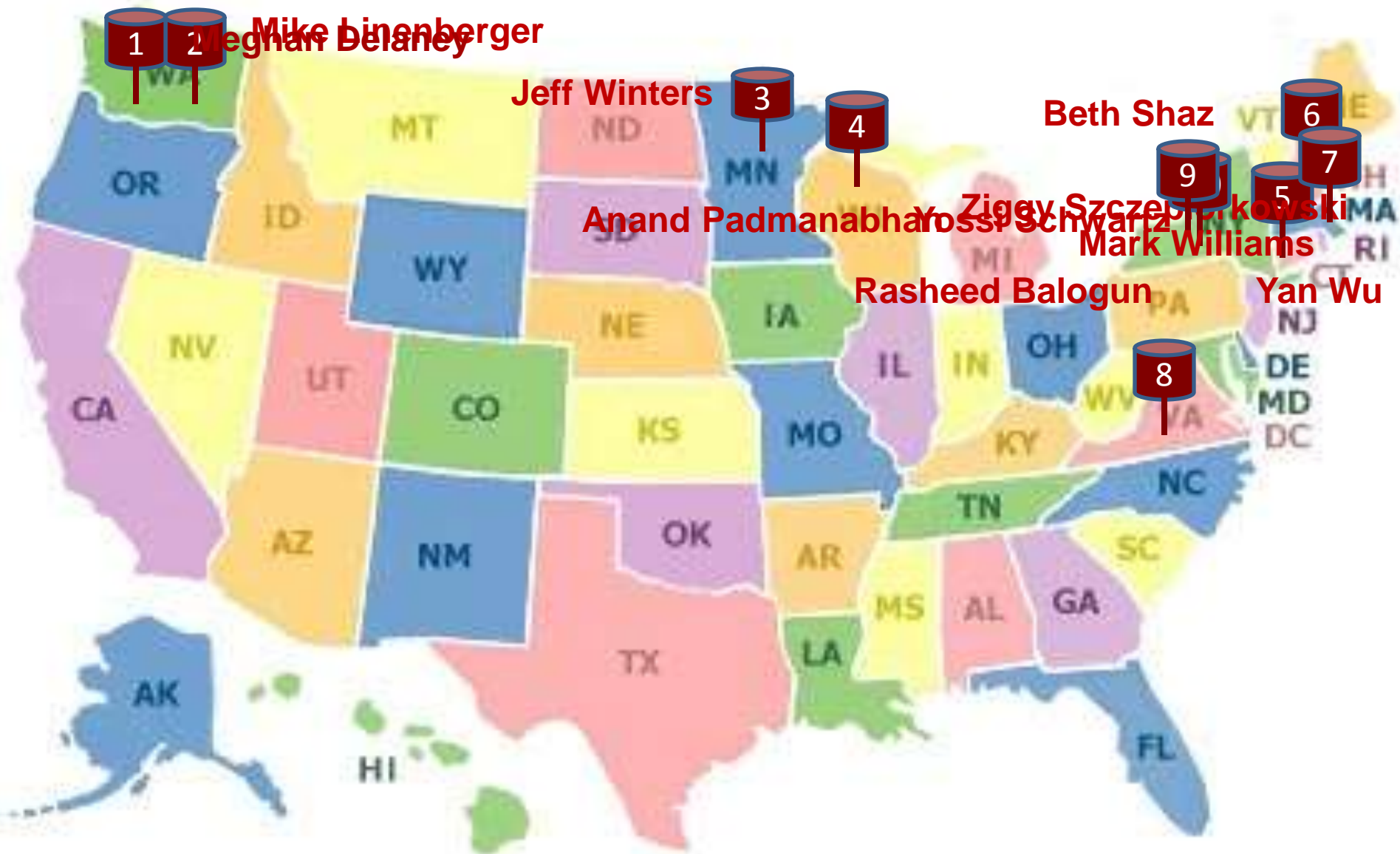
It Takes a Nation...



Additional Facts about the 2013 Guidelines

- Internationally recognized
 - Translated into Spanish and Russian
 - Adopted and endorsed by the Spanish Hematology Society
- Utilized by third party payers for determining coverage of apheresis procedures

It Takes a Nation...



JCA 2013 Committee Denver CO Fall 2012



Future Directions for the Guidelines

- 7th edition of guidelines to be published in June of 2016
- Expansion of references reviewed in creating the fact sheets
- Guidance for the use of apheresis in additional disorders including: **93 conditions being considered. Seattle, next week**
 - HELLP (hemolysis, elevated liver enzymes, low platelet ct)
 - TMA, complement-mediated TMA, metabolism-mediated TMA, coagulation-mediated TMA
 - Shiga toxin-mediated (ST-HUS)
 - Hemophagocytic lymphohistiocytosis/ hematophagocytosis syndrome

Expansion of translation into other languages (6th Issue)

- Spanish and Russian
- Simplified Chinese

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