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PEARLS OF LABORATORY MEDICINE

Peripheral Blood Stem Cell Collection

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CCTC Clinical Chemistry Trainee Council

Peripheral Blood Stem Cell (PBSC) Collection

Hematopoietic stem cells are pluripotent stem cells that are responsible for the formation of blood cells, and, are collected for transplantation. Hematopoietic stem cell transplantation is often referred to as bone marrow transplantation and more aptly as hematopoietic progenitor cell (HPC) transplantation.

Objectives:

- Why we perform PBSC collections?
- How we perform PBSC collections?
- When we perform PBSC collections?

Indications for Hematopoietic Progenitor Cell Transplantation (HPCT)

HPCT is a widely accepted treatment strategy for most hematological malignancies, certain non-hematological malignancies and for several non-malignant conditions

HPCT includes Allogeneic and Autologous HPCT

- Multiple Myeloma / Plasma Cell Dyscrasia
- Non Hodgkin's Lymphoma
- Acute myeloid leukemia (AML)
- Hodgkin disease
- Acute lymphocytic leukemia (ALL)
- Myelodysplastic syndrome (MDS) / Myeloproliferative disorders (MPD)
- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)
- Aplastic Anemia
- Solid tumors e.g. Germ Cell, Ewing's sarcoma, neuroblastoma
- Hemoglobinopathies
- Immune deficiency syndromes
- Some autoimmune and Immune dysregulation disorders

Autologous vs. Allogeneic HPCT

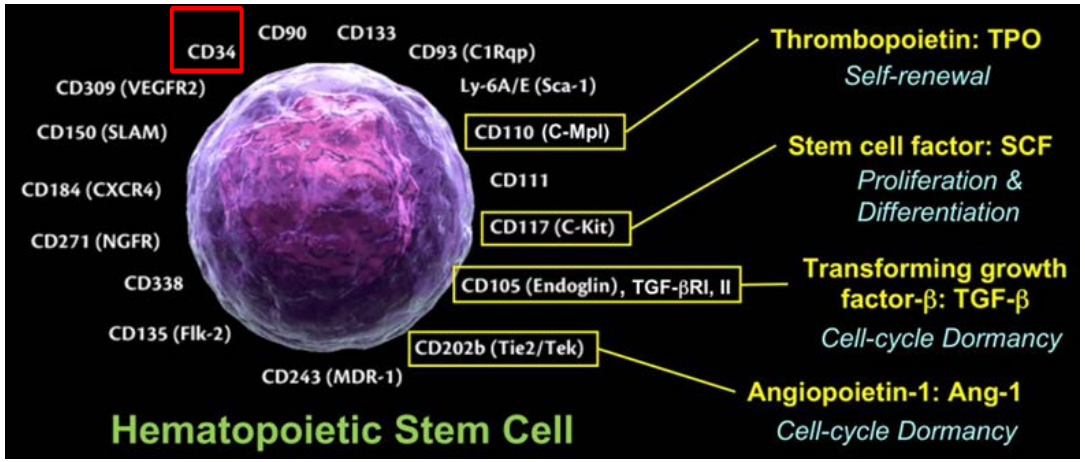
Autologous HPCT

- To allow for bone marrow recovery after provision of high-dose chemotherapy
- Regimens do not include immunosuppression
- Patients undergo HPC collection

Allogeneic HPCT

- To replace diseased marrow with normal bone marrow from a healthy donor – For graft versus tumor effect via T- lymphocytes
- Regimens contain immunosuppression
- Healthy related or unrelated donors undergo HPC collection

Human Progenitor Cells



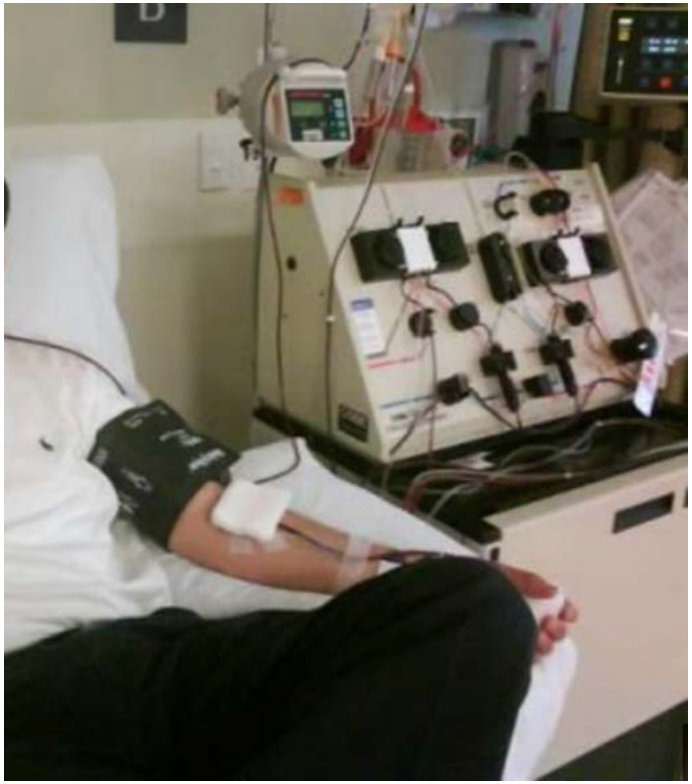
CD34 serves as a marker for HPC

CD34+ Cells - Predictor of Stable Engraftment

American Society for Blood and Marrow Transplantation (ASBMT) consensus guidelines (2014):

- 2x10^6 CD34+cells/kg accepted as minimum threshold however 5x10^6CD34+ cells/kg recipient weight optimal for Auto HPCT
- 2x10^6 CD34+cells/kg accepted as minimum threshold however 4-5x10^6CD34+ cells/kg recipient weight probably ideal for Allo HPCT

Stem Cell Procurement



Peripheral Blood Progenitor Cell Collection

Bone Marrow Harvest

Umbilical Cord Blood Collection

PB vs BM HPC collection

Peripheral Blood

- Larger numbers of CD34+ and CD3+ cells
  - Shorter duration of cytopenias
  - Enhanced immune reconstitution
  - Reduced morbidity

However

  - Increased chronic GVHD
- May require central venous access
- Side effects growth factors, chemotherapy, anticoagulant

Bone Marrow

- Surgical procedure GA / spinal
- Pain during recovery
- Less chronic GVHD

Median per kg	Bone Marrow	Peripheral Blood	P Value
Total nucleated cells (TNC) x 10^8	2.3	11.6	0.001
CD34 x 10^6	2.4	7.3	0.001
CD x 10^3	23.8	279	0.001
Volume ml	12.2	4	0.001

Bensinger et al NEJM, 2001 344;175

Peripheral Blood Progenitor Cell collection

Center for International Blood and Marrow Transplant Research Transplant Activity Report Covering 2010-2014

	DONOR TYPE							
	Autologous		Related		Unrelated		Grand Total	
CELL SOURCE	N	%	N	%	N	%	N	%
Bone Marrow	172	<1	3,923	24	4,515	20	8,610	9
Cord Blood	521	1	90	1	4,100	18	4,711	5
Peripheral Blood	52,076	97	12,244	75	14,429	63	78,749	85
Data not available*	709	1	0	0	5	<1	714	1
Grand Total	53,478	100	16,257	100	23,049	100	92,784	100

HPC Recovery from Peripheral Blood

HPC collection from peripheral blood results from the combination of:

- Effective mobilization procedures
- Efficient apheresis techniques

Mobilization Regimens

- Chemotherapy +/-G-CSF
- Cytokines:

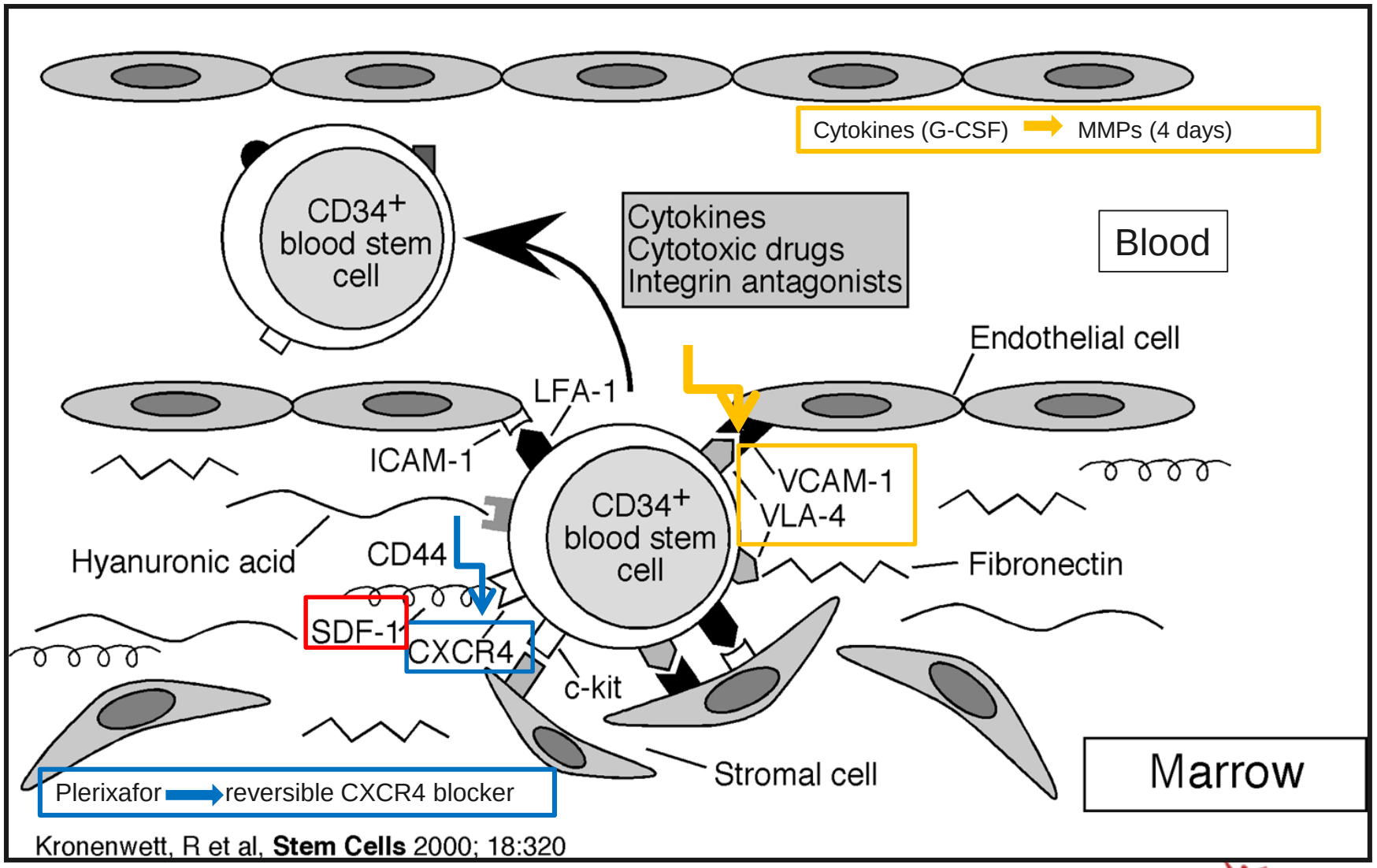
Granulocyte Colony Stimulating Factor (G-CSF)

filgrastim / lenograstim

GM-CSF

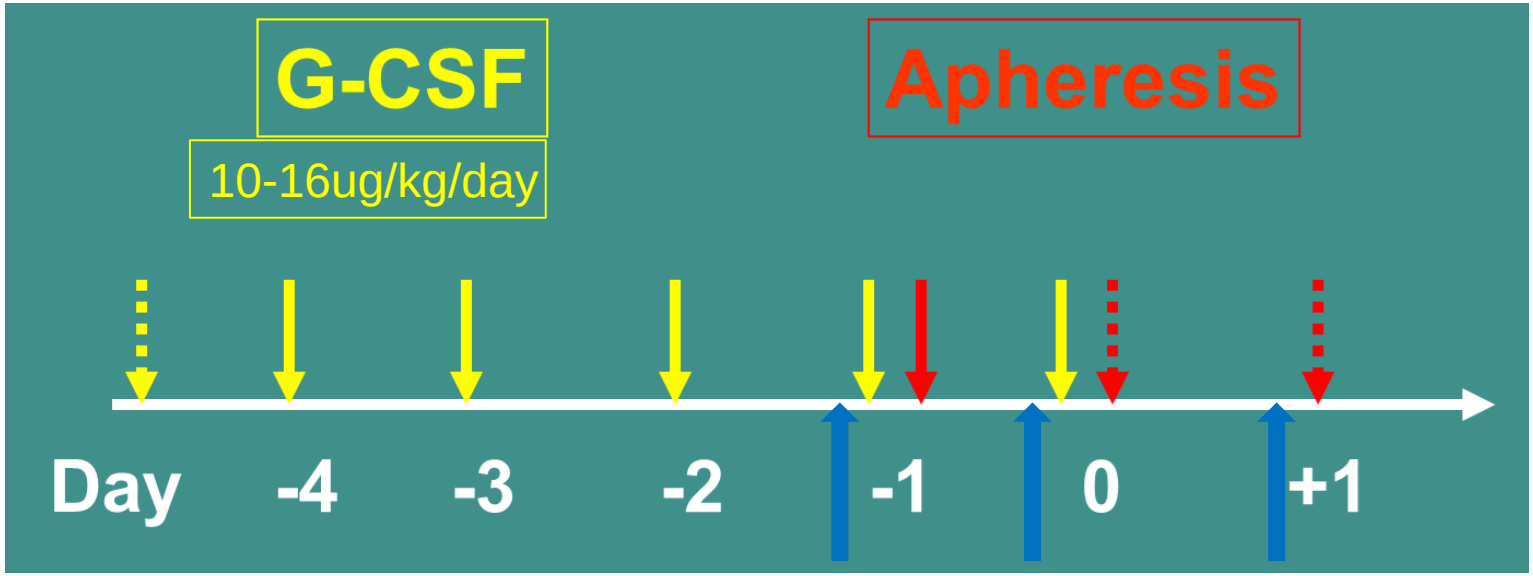
sargramostim

- Novel agents:
  Plerixafor (Mozobil®) +/-G-CSF



Kronenwett, R et al, **Stem Cells** 2000; 18:320

PBSC Mobilization and Apheresis



Pleriaxafor
240ug/kg/day

Side effects of GCSF

Common

Musculoskeletal Pain, “Flu-like”, Arthralgia, Headache

Nausea

Malaise, fatigue

Splenomegaly

Mild thrombocytopenia

Increase LDH, Increase Alk Phos

Uncommon:

Fever, Rash, Arthritis

Rare:

Severe Thrombocytopenia,

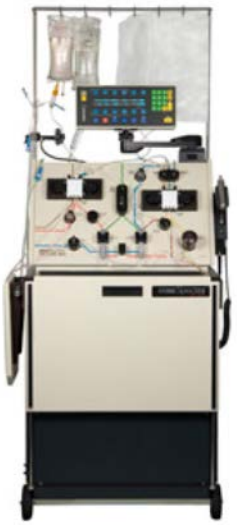
Splenic Rupture/ Bleed

Thrombosis

CD34+ collection in randomized trials of GCSF vs GCSF and Plerixafor (Mozobil®)

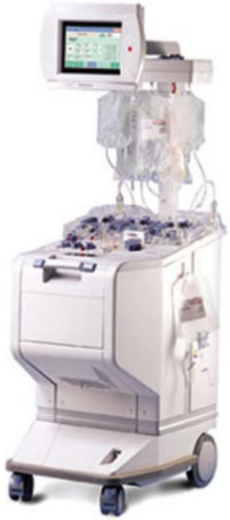
- Adverse events with Plerixafor include GI disorders and injection site reactions.
- Earlier randomized studies demonstrated a higher % of myeloma patients reaching 6x10^6 CD34+ cells/kg with Plerixafor and G-CSF compared to G-CSF mobilized patients alone. Median number of days to reach ≥ 6 x 10^6 CD34+ cells/kg was one day vs four days for GCSF alone.
- Additional randomized study in NHL demonstrated a higher % of patients reaching 5x10^6 CD34+ cells/kg using Plerixafor and GCSF vs GCSF alone.
- Cost is a limiting factor for the use of Plerixafor

Commonly used Apheresis Blood Cell Separators



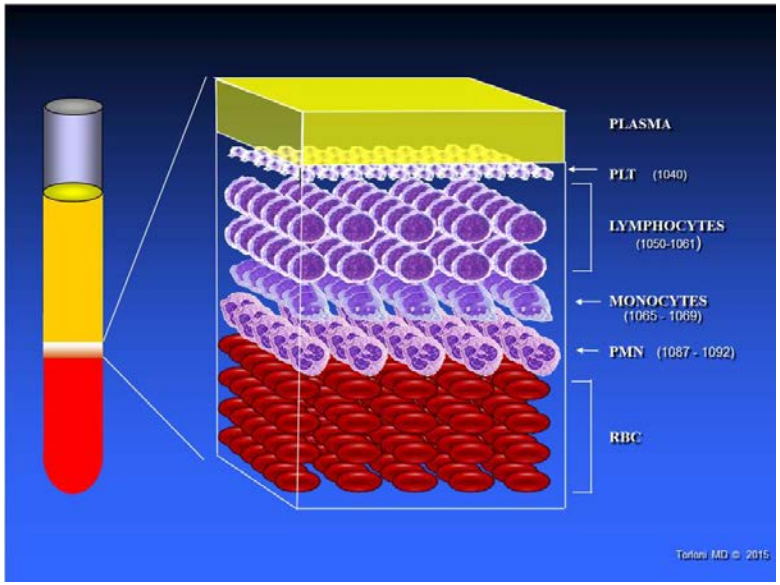
COBE Spectra

Spectra Optia



Amicus

Separation by density centrifugation



Courtesy of Sergio Torloni, MD

Side effects of Venous Access and Apheresis

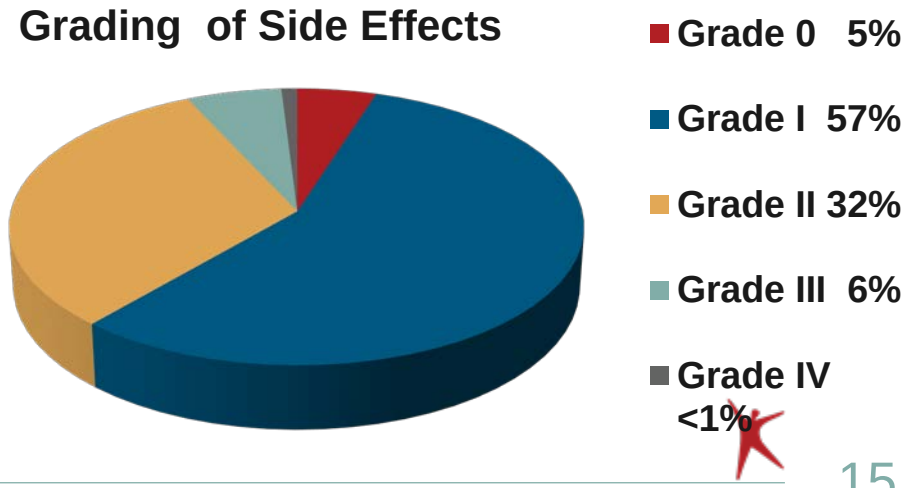
NMDP prospective trial n=2408

51% Hypocalcemia / Citrate toxicity

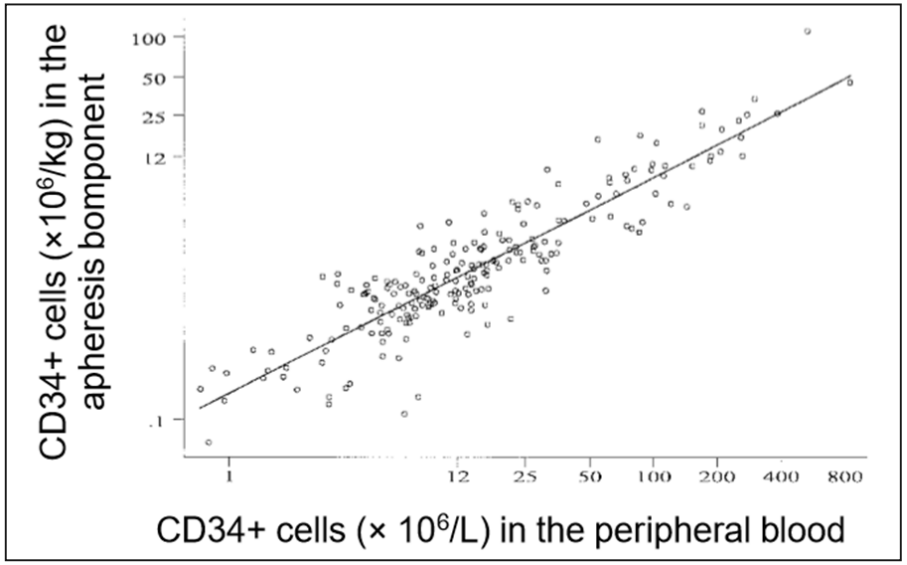
20% Nausea

22% Venous Access issues (IV lines infiltrated, multiple attempts, hematomas, poor flow)

1-6% Other –pain, chills, hyper/hypotension



Circulating CD34+ cell numbers are predictive of collected CD34+ cell numbers



Yu J et al, Transfusion, 1999

Collection Efficiency (CE) = Cells in the collection bag / Cells through the apheresis device

Maximizing collection based on instrument efficiency and donor peripheral CD34+ cell counts can be performed using Predictive Algorithms

Predictive Algorithms

$$\text{CD34+ cells to be collected per liter (L) of processed blood} = \frac{\text{peripheral blood CD34+ cells/L X CE}}{\text{Body weight in kilograms (kg)}}$$

Rationale For CD34-based Collections

- Worldwide Industry Standard Practice
- Ability to project expected cell yield
- Ability to reduce apheresis time
- Process less total blood volume (TBV) to collect the same CD34+ dose

$$\textbf{TBV to process (L)} = \frac{\textbf{Target number of CD34 cells to be collected x recipient weight (kg)}}{\textbf{Peripheral blood CD34+ cells x 0.3* (CE)}}$$

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Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

- **Employment or Leadership**: No disclosures
- **Consultant or Advisory Role:** No disclosures
- **Stock Ownership:** No disclosures
- **Honoraria:** No disclosures
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- **Patents:** No disclosures

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