

# Rode bloedcel morfologie: Van Labo tot Kliniek

Critically Appraised Topic

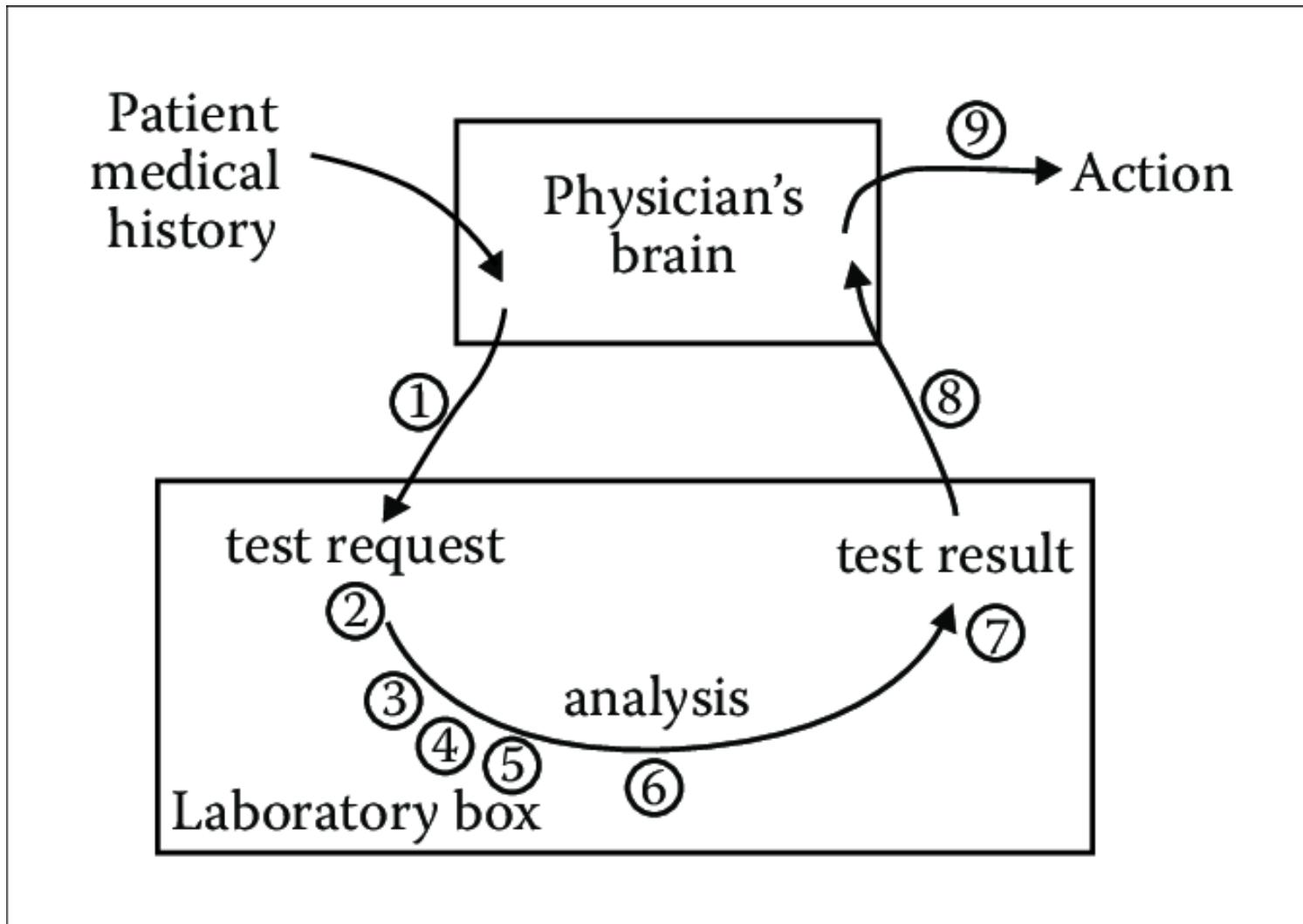
# Doel CAT

- ▶ Evaluatie van
  - ▶ Klinische relevantie van de rode bloedcelmorfologie
  - ▶ Kennis en gebruik van de rode bloedcelmorfologie door clinici
  - ▶ Rapportering van rode bloedcel morfologie
- ▶ Ter verbetering van
  - ▶ Workflow laboratorium AZ Delta
  - ▶ Dienstverlening tav clinici
  - ▶ Zorg voor patiënten

# Indeling

- ▶ 1) Inleiding
  - ▶ Rapportering
  - ▶ Morfologie
  - ▶ Werkwijze AZ Delta
- ▶ 2) Vragen
  - ▶ Wat zijn de klinische contexten waarbij afwijkingen in de morfologie van de rode reeks voorkomen?
  - ▶ Hoe nuttig vinden de clinici de morfologie van rode bloedcellen?
  - ▶ Hoe moet de morfologie van rode bloedcellen gerapporteerd worden?
- ▶ 3) Conclusie en To do's

# Klinisch/diagnostisch scenario - Rapportering



# Klinisch/diagnostisch scenario - RBC

## Morfologie

- ▶ Basis hematologisch onderzoek
  - ▶ Controle van afwijkende resultaten automatische cel analyzer
  - ▶ Diagnostische argumenten voor etiologie anemie
    - ▶ Hemolytisch:
      - ▶ Fragmentocyten: TMA?
      - ▶ Ovalocyten/spherocyten: Congenitaal?
    - ▶ Microcytair:
      - ▶ Basofiele stippling: Lood intoxicatie
      - ▶ Thalassemie
    - ▶ Macrocytair
      - ▶ Leverlijden
      - ▶ Myelodysplasie
      - ▶ Megaloblastische anemie: Vit B12 deficientie
  - ▶ Diagnostische argumenten voor andere pathologie

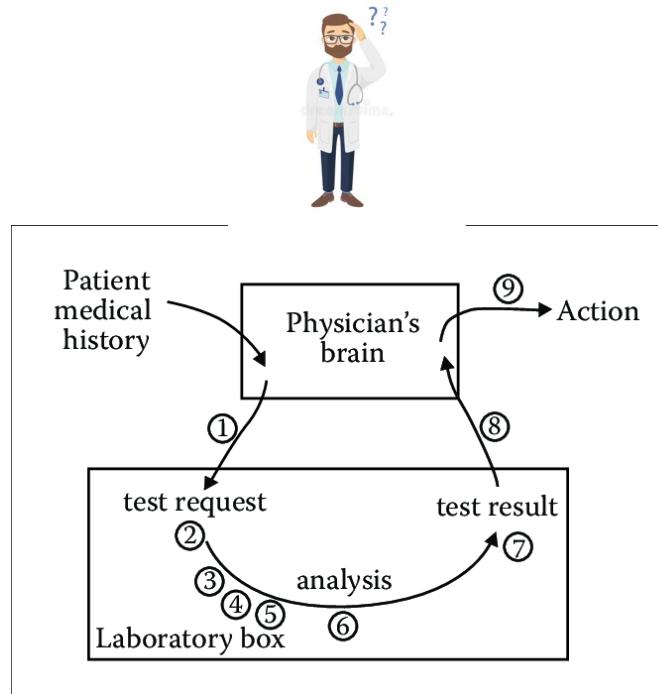
# Klinisch/diagnostisch scenario - RBC Morfologie



- ▶ Voordelen PBS
  - ▶ Relatief snel uitvoerbare analyse
  - ▶ Hoewel minder specifiek, vaak reeds richtinggevend voor DD/therapie
  - ▶ Zeer veel informatie
  
- ▶ Nadelen PBS
  - ▶ Zelden Pathognomisch
  - ▶ Arbeidsintensief
  - ▶ Interobserver variatie
  - ▶ Uitstrijkartefacten

# Inleiding- AZ Delta

- ▶ Schaal
  - ▶ 18.000 EDTA stalen/maand (Compleet + Diff)
  - ▶ 2.200 (12%) met microscopisch nazicht
    - ▶ 97% Aangevraagd door labo
    - ▶ 3% Aangevraagd door clinici
- ▶ Workflow
  - ▶ Uitstrijkjes door SP-10 Module gemaakt (of manueel)
  - ▶ Inlezen digitale microscoop (DM96 Cellavision)
  - ▶ Evaluatie kwaliteit uitstrijkje + gescand gebied
  - ▶ Gradering afwijkingen op DM96 of manuele beoordeling RBC



RBC Morphology	AZ Delta				
	Present	Rare	1+	2+	3+
Acanthocyte	>3	/	/	/	/
Anisocytosis	>3	/	/	/	/
Anulocyte	>3	/	/	/	/
Echinocyte	>3	/	/	/	/
Elliptocyte	>3	/	/	/	/
Hypochromasia	>3	/	/	/	/
Macrocytosis	>3	/	/	/	/
Microcytosis	>3	/	/	/	/
Ovalocyte	>3	/	/	/	/
Poikilocytosis	>3	/	/	/	/
Polychromasie	>3	/	/	/	/
Sickle cell / drepanocyte	>3	/	/	/	/
Stomatocyte	>3	/	/	/	/
Target cell	>3	/	/	/	/
Dimorphism	>3	/	/	/	/
Pappenheimer bodies	>1	/	/	/	/
Howell-Jolly body	>1	/	/	/	/
Basophilic stippling	>1	/	/	/	/
Teardrop cell/ dacrocute	/	1-3	4-10	11-20	>20
Spherocyte	/	1-3	4-10	11-20	>20
Schistocyte/fragmentocyte	/	1-3	4-10	11-20	>20
Rouleaux	If present	/	/	/	/
Agglutination	If present	/	/	/	/
Parasites	If present	/	/	/	/
*All counts per 1000 RBC					

# Vraag 1: Relevante klinische contexten van de rode bloedcelmorphologie?



# Vraag 2: Hoe ervaren clinici het gebruik van de rode bloedcelmorphologie?

- ▶ Enquête binnen AZ Delta en Sint Andries
  - ▶ Gebruik van RBC-Indices
    - ▶ “Altijd”, “Vaak >50%”, “Soms 15-50%”, “Zelden <15%”, “Nooit”
  - ▶ Gebruik van RBC-Morfologie
    - ▶ “Altijd”, “Vaak >50%”, “Soms 15-50%”, “Zelden <15%”, “Nooit”
  - ▶ Inschatting van klinische nut van morfologische afwijkingen
    - ▶ “Zeer nuttig”, “nuttig”, “zelden nuttig”, “niet nuttig”, “niet gekende term”
- ▶ Analyse
  - ▶ Beschrijvende statistiek
  - ▶ Opstellen subgroep analyse
  - ▶ Groepering antwoorden klinisch nut

# Resultaten enquête

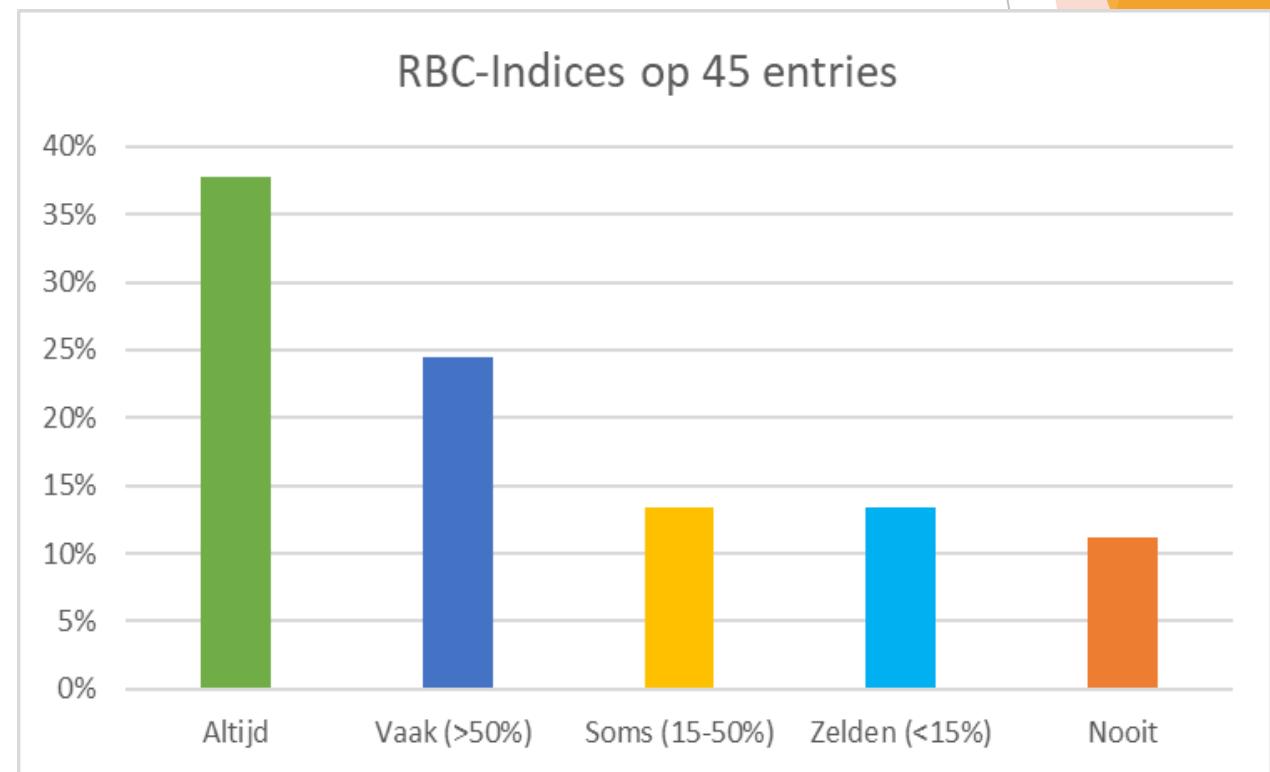
- ▶ 45 antwoorden op 361 mails
- ▶ Verdeling van specialisaties:
  
- ▶ Subgroepen:
  - ▶ 17 Inwendige specialisaties
  - ▶ 7 Heelkundige specialisaties
  - ▶ 21 Overige specialisaties

Lijst van specialisaties:	Aantal
Gynaecologie	5
Pediatrie	5
MDL/gastro	5
Orthopedie	4
Anesthesie	3
Neurologie	3
Oncologie	3
Geriatrie	2
Psychiatrie	2
Urgentie/spoed	2
Pneumologie	2
Neurochirurgie	1
Hematologie	2
Nefrologie	1
Algemene heelkunde	1
ASO inwendige	1
Reumatologie	1
Vaatheelkunde	1
Niet ingevuld	1

# Resultaten survey

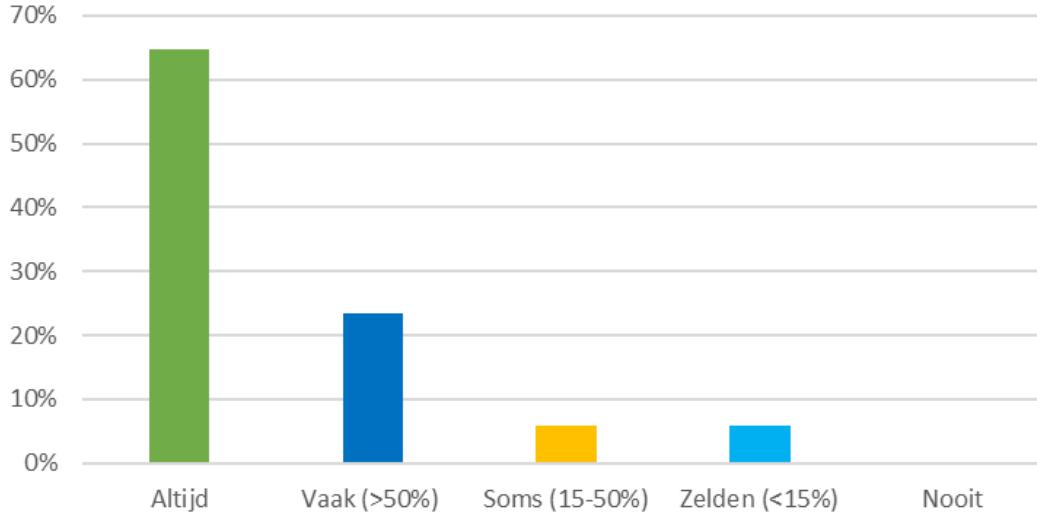
- ▶ Indien u de resultaten van een completestraal (CBC) bekijkt, hoe vaak kijkt u naar de rode bloedcel indices buiten hematocriet en hemoglobine? (bv. MCV, MCHC, RDW)

Altijd	17	38%
Vaak (>50%)	11	24%
Soms (15-50%)	6	13%
Zelden (<15%)	6	13%
Nooit	5	11%



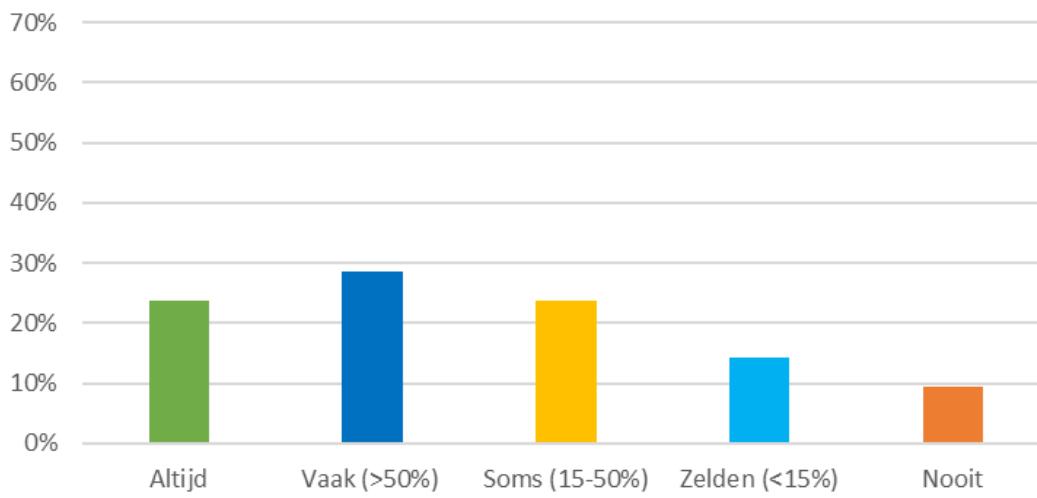
Altijd	11	65%
Vaak (>50%)	4	24%
Soms (15-50%)	1	6%
Zelden (<15%)	1	6%
Nooit	0	0%

RBC-Indices op 17 Inwendige specialisaties



Altijd	5	24%
Vaak (>50%)	6	29%
Soms (15-50%)	5	24%
Zelden (<15%)	3	14%
Nooit	2	10%

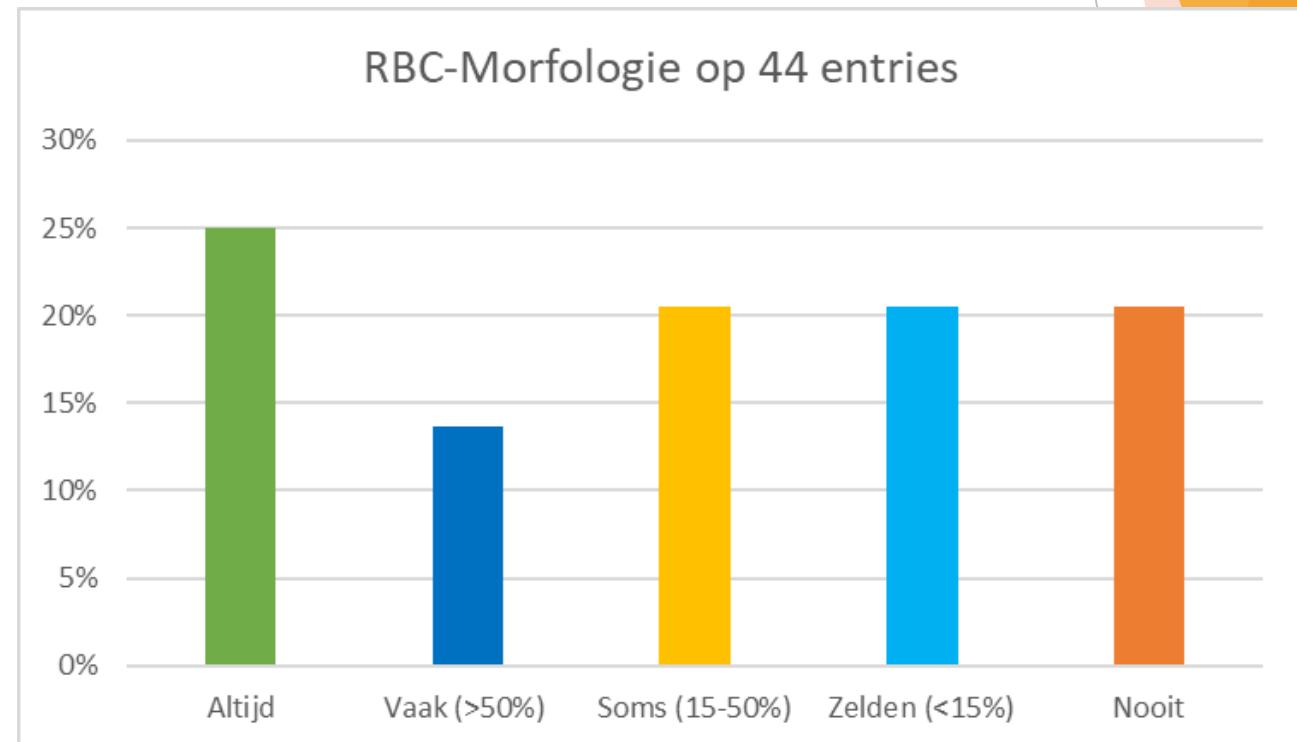
RBC-Indices op 21 niet heelkundige, niet inwendige specialisaties



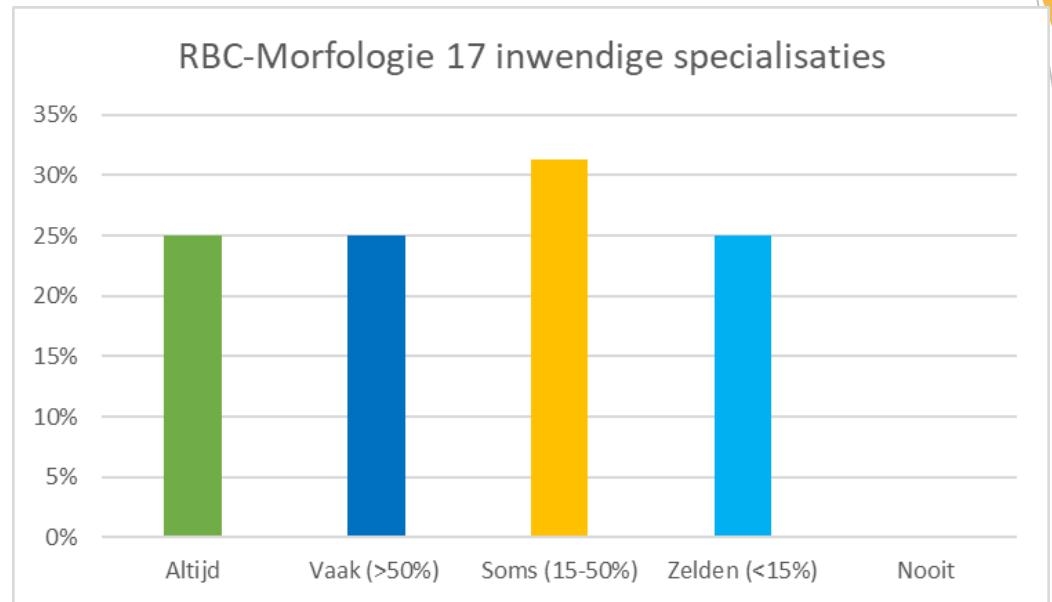
# Resultaten survey

- ▶ Hoe vaak bekijkt u de beschrijving van de rode bloedcel morfologie? (indien aanwezig)

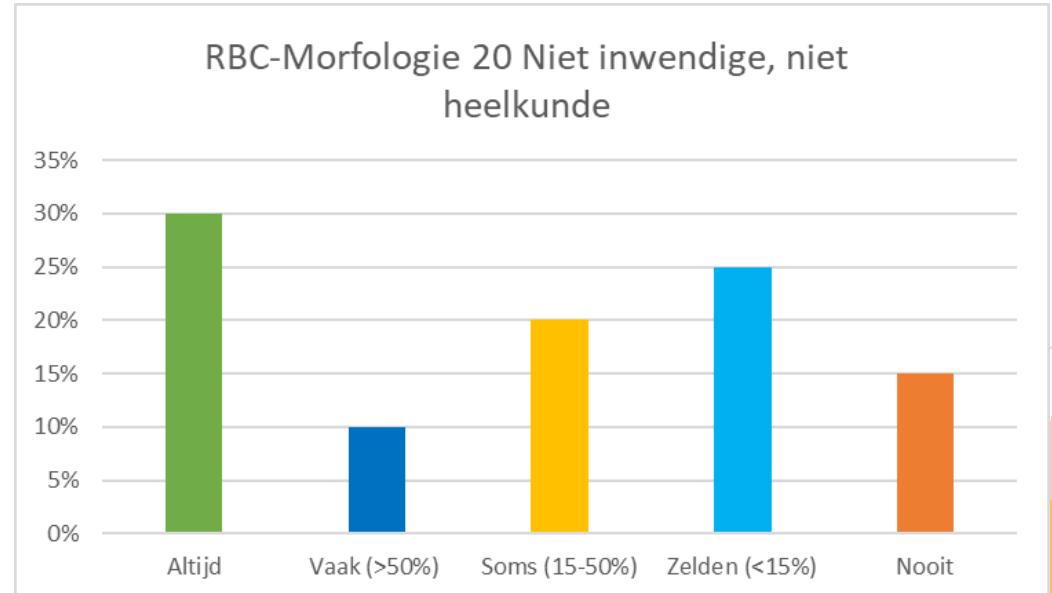
Altijd	11	25%
Vaak (>50%)	6	14%
Soms (15-50%)	9	20%
Zelden (<15%)	9	20%
Nooit	9	20%



Altijd	4	25%
Vaak (>50%)	4	25%
Soms (15-50%)	5	31%
Zelden (<15%)	4	25%
Nooit	0	0%



Altijd	6	30%
Vaak (>50%)	2	10%
Soms (15-50%)	4	20%
Zelden (<15%)	5	25%
Nooit	3	15%



All Clinicians (n=37)	Useful	Less useful	Unknown term
Microcytosis	62%	32%	6%
Macrocytosis	61%	33%	6%
Sickle cell / Drepanocyte	52%	33%	15%
Schistocyte / Fragmentocyte	45%	36%	18%
Spherocyte	30%	39%	30%
Anisocytosis	21%	38%	41%
Acanthocyte / Spur cell	21%	29%	50%
Hypochromasia	19%	47%	34%
Target cell	18%	21%	61%
Howell-Jolly body	18%	30%	52%
Rouleaux	16%	44%	41%
Tear drop cell / Dacrocyte	15%	18%	67%
Agglutination	15%	48%	36%
Stomatocyte	12%	27%	61%
Echinocyte	9%	18%	73%
Elliptocyte	9%	24%	67%
Poikilocytosis	9%	45%	45%
Pappenheimer bodies	6%	18%	76%
Anulocyte	6%	24%	70%
Basophilic stippling	6%	24%	70%
Nucleated red blood cell	6%	36%	58%
Ovalocyte	6%	39%	55%
Polychromasia	6%	39%	55%
Dimorphism	3%	30%	67%

Internal medicine (n=14)	Useful	Less useful	Unknown term
Microcytosis	77%	23%	0%
Macrocytosis	77%	23%	0%
Sickle cell / Drepanocyte	69%	23%	8%
Schistocyte / Fragmentocyte	69%	23%	8%
Spherocyte	42%	25%	33%
Anisocytosis	29%	36%	36%
Acanthocyte / Spur cell	36%	36%	29%
Hypochromasia	17%	67%	17%
Target cell	33%	33%	33%
Howell-Jolly body	31%	38%	31%
Rouleaux	25%	67%	8%
Tear drop cell / Dacrocyte	33%	33%	33%
Agglutination	31%	31%	38%
Stomatocyte	31%	38%	31%
Echinocyte	15%	38%	46%
Elliptocyte	15%	38%	46%
Poikilocytosis	14%	57%	29%
Pappenheimer bodies	15%	31%	54%
Anulocyte	15%	31%	54%
Basophilic stippling	15%	38%	46%
Nucleated red blood cell	15%	46%	38%
Ovalocyte	15%	46%	38%
Polychromasia	8%	50%	42%
Dimorphism	8%	42%	50%

Non-Internal medicine (n=23)	Useful	Less useful	Unknown term
Microcytosis	52%	38%	10%
Macrocytosis	50%	40%	10%
Sickle cell / Drepanocyte	30%	45%	25%
Schistocyte / Fragmentocyte	40%	40%	20%
Spherocyte	10%	25%	65%
Anisocytosis	10%	30%	60%
Acanthocyte / Spur cell	24%	48%	29%
Hypochromasia	5%	60%	35%
Target cell	15%	40%	45%
Howell-Jolly body	10%	25%	65%
Rouleaux	20%	35%	45%
Tear drop cell / Dacrocyte	13%	17%	70%
Agglutination	10%	14%	76%
Stomatocyte	5%	10%	86%
Echinocyte	0%	20%	80%
Elliptocyte	0%	15%	85%
Poikilocytosis	0%	24%	76%
Pappenheimer bodies	5%	5%	90%
Anulocyte	5%	15%	80%
Basophilic stippling	0%	30%	70%
Nucleated red blood cell	0%	35%	65%
Ovalocyte	0%	10%	90%
Polychromasia	5%	37%	58%
Dimorphism	5%	33%	62%

# Besluit Enquête

- ▶ Slechts 1/3 kijkt naar rapport morfologie als dit voorzien is
- ▶ Meerderheid clinici niet bekend met meerdere termen
  - ▶ Wel ‘goed’ gekend
    - ▶ Microcytose
    - ▶ Macrocytose
    - ▶ Sickle cells
    - ▶ Fragmentocyten
- ▶ Indien wel gekend eerder als niet nuttig ervaren
- ▶ Gelijkaardige resultaten als 2 recente enquêtes uit de literatuur

- 1) Newman AW, Rishniw M, Behling-Kelly E. Reporting and interpreting red blood cell morphology: Is there discordance between clinical pathologists and clinicians? *Vet Clin Pathol.* 2014 Dec;1;43(4):487-95.
- 2) Ford JC, Milner R, Dix DB. Red blood cell morphology reporting: How much is a waste of time? *J Pediatr Hematol Oncol.* 2011 Jan;33(1):10-4.

# Ter vergelijking: Ford JC 2011

- ▶ Studie inzake pediatrische hematologie
  - ▶ 515 mails verstuurd, 129 antwoorden
    - ▶ 78 artsen, 51 studenten

**TABLE 3.** Responses to Overall Questions About RBC Morphology Reporting

Question	“Always” or “Frequently” (%)	“Sometimes” or “Rarely”
In general, I review the RBC indices other than hemoglobin (eg, MCV, MCH)	80.6	19.4
When I review a patient’s CBC, I refer to the RBC morphology section	70.5	29.5
I find that the information from the RBC morphology section is clinically useful	47.3	52.7

**TABLE 4.** Proportion of All Respondents Describing Each RBC Morphology as Clinically Useful

RBC Morphology	% Useful
Sickle cells	95.3
Malaria parasites seen	91.4
Howell Jolly bodies	83.5
Microcytosis	82.8
Macrocytosis	82.5
Spherocytes	81.9
Schistocytes	77.8
Target cells	75.6
Hypochromasia	70.5
Basophilic stippling	63
Elliptocytes	48
Acanthocytes	46.8
Rouleaux	46
Teardrop forms	46
Poikilocytosis	44.4
RBC agglutination	42.4
Stomatocytes	42
Polychromasia	41.9
Anisocytosis	40
Echinocytes	30.6
Pappenheimer bodies	25.4
Abnormally constricted cells	21.8

RBC indicates red blood cell.

1) Ford JC, Milner R, Dix DB. Red blood cell morphology reporting: How much is a waste of time? *J Pediatr Hematol Oncol.* 2011 Jan;33(1):10-4.

# Vraag 3: Hoe moet de morfologie van RBC gerapporteerd worden?

- ▶ Typisch bestaat RBC morfologie rapport uit 1-2 delen:
  - ▶ 1) Beoordeling prevalentie afwijking:
    - ▶ Kwalitatief
      - ▶ Aanwezig - Afwezig
    - ▶ Kwantitatief
      - ▶ Bv fragmentocytentelling
    - ▶ Semi-kwantitatief
      - ▶ Gradering
  - ▶ 2) Samenvattende beschrijving / commentaar

Palmer, L., Briggs, C., McFadden, S., Zini, G., Burthem, J., Rozenberg, G., Proytcheva, M. and Machin, S.J. (2015), ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features. Int. Jnl. Lab. Hem., 37: 287-303.

# Gradering RBC

RBC Morphology	Uzleuven					ICSH 2015				Constantino et al 2014				VHL werkgroep - "Difboekje" 2013			
	Present	Rare	1+	2+	3+	Present	Few/1+	2+	3+	Present	1+/Few	2+/Moderate	3+/Marked	Present	1+	2+	3+
Acanthocyte	/	1-3	3-10	11-20	>20	/	/	50-200	>200	/	10-100	110-300	>300	/	50-200	200-500	>500
Anisocytosis	/	/	/	/	/	/	/	110-200	>200	/	/	/	/	/	/	/	/
Anulocyte	/	1-3	3-10	11-20	>20	/	/	/	/	/	/	/	/	/	/	/	/
Echinocyte	/	/	6-20	>20	>40	/	/	50-200	>200	If >300	/	/	/	/	50-200	200-500	>500
Elliptocyte	/	/	3-10	11-20	>20	/	/	50-200	>200	/	60-200	210-500	>500	/	50-200	200-500	>500
Hypochromasia	/	/	10-40	40-125	>125	/	/	110-200	>200	/	50-150	160-400	>400	/	50-200	200-500	>500
Macrocytosis	/	/	10-40	40-125	>125	/	/	110-200	>200	/	/	/	/	If present	/	/	/
Microcytosis	/	/	10-40	40-125	>125	/	/	110-200	>200	/	/	/	/	If present	/	/	/
Ovalocyte	/	/	6-20	>20	>40	/	/	50-200	>200	/	60-200	210-500	>500	/	50-200	200-500	>500
Poikilocytosis	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Polychromasie	/	/	3-10	11-20	>20	/	/	50-200	>200	/	30-50	60-200	>200	/	50-200	200-500	>500
Sickle cell / drepanocyte	/	/	1-3	3-7	>7	/	/	10-20	>20	If present	/	/	/	If >10	/	/	/
Stomatocyte	/	/	3-10	11-20	>20	/	/	50-200	>200	If >300	/	/	/	/	50-200	200-500	>500
Target cell	/	/	/	/	/	/	/	50-200	>200	/	50-100	110-250	>250	/	5-20	20-50	>50
Dimorphism	/	/	/	/	/	If present	/	/	/	If present	/	/	/	/	/	/	/
Pappenheimer bodies	/	/	1-3	3-7	>7	/	/	20-30	>30	If present	/	/	/	if present	/	/	/
Howell-Jolly body	/	/	1-3	3-7	>7	/	/	20-30	>30	If present	/	/	/	/	50-200	200-500	>500
Basophilic stippling	/	/	1-3	3-7	>7	/	/	50-200	>200	/	/	/	/	/	50-200	200-500	>500
Teardrop cell/ dacrocute	/	/	3-10	11-20	>20	/	/	50-200	>200	if >40	/	/	/	/	5-20	20-50	>50
Spherocyte	/	1-3	3-10	11-20	>20	/	/	50-200	>200	/	10-50	60-200	>200	/	50-200	200-500	>500
Schistocyte/fragmentocyte	/	/	3-10	11-20	>20	/	<10	10-20	>20	/	10-50	60-150	>150	/	5-20	20-50	>50
Rouleaux	If present	/	/	/	/	If present	/	/	/	/	/	110-500	>500	/	50-200	200-500	>500
Agglutination	If present	/	/	/	/	If present	/	/	/	If present	/	/	/	/	50-200	200-500	>500
Parasites	If present	/	/	/	/	If present	/	/	/	If present	/	/	/	If present	/	/	/

\*All counts per 1000 RBC

# Gradering RBC

- ▶ Heterogeniteit!
  - ▶ Ondanks meerdere pogingen tot standaardisatie
  - ▶ Ondanks toenemende standaardisatie in laboratorium
- ▶ Reden?
  - ▶ Onvoldoende evidence over gebruik verschillende graderingsystemen
  - ▶ Onvoldoende studies over prevalentie afwijkingen
    - ▶ Specifieke ziektes
    - ▶ Gezonde populatie

- 1) Walton JR. Uniform grading of hematologic abnormalities. Am J Med Technol. 1973 Dec;39(12):517-23
- 2) Palmer, L et al. ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features. Int. Jnl. Lab. Hem., 37: 287-303

# International council of standardization in hematology - 2015

- ▶ Consensus richtlijn
- ▶ Poging tot standaardisatie
  - ▶ Terminologie
  - ▶ Gradering
- ▶ Vermijden van 1+ gradatie
  - ▶ Vaak aspecifiek voorkomen of klinisch weinig relevant
  - ▶ Uitz. Fragmentocyten

## ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features.

Palmer L<sup>1</sup>, Briggs C, McFadden S, Zini G, Burthem J, Rozenberg G, Proytcheva M, Machin SJ.

 Author information

### Abstract

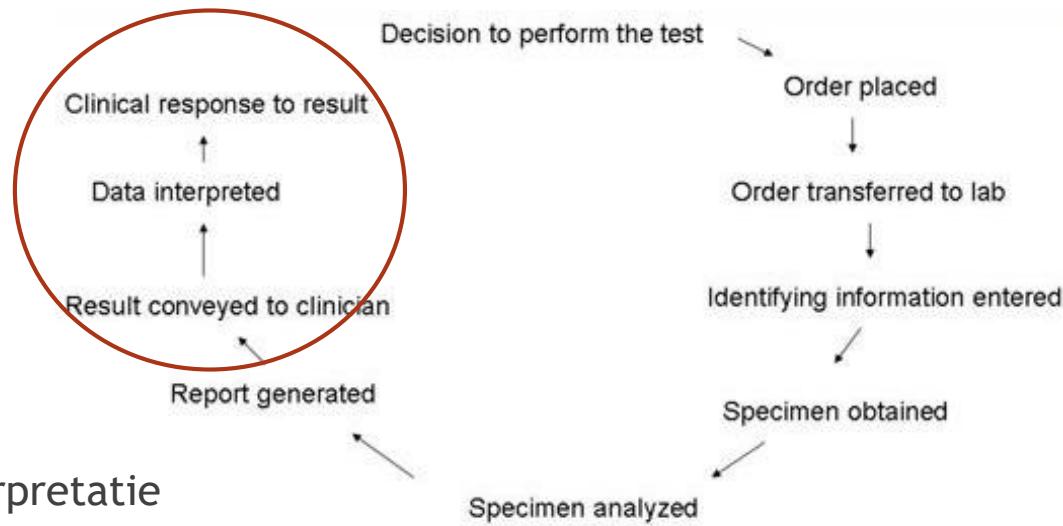
These guidelines provide information on how to reliably and consistently report abnormal red blood cells, white blood cells and platelets using manual microscopy. Grading of abnormal cells, nomenclature and a brief description of the cells are provided. It is important that all countries in the world use consistent reporting of blood cells. An international group of morphology experts have decided on these guidelines using consensus opinion. For some red blood cell abnormalities, it was decided that parameters produced by the automated haematology analyser might be more accurate and less subjective than grading using microscopy or automated image analysis and laboratories might like to investigate this further. A link is provided to show examples of many of the cells discussed in this guideline.

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RBC Morphology	ICSH 2015			
	Present	Few/1+	2+	3+
Acanthocyte	/	/	50-200	>200
Anisocytosis	/	/	110-200	>200
Anulocyte	/	/	/	/
Echinocyte	/	/	50-200	>200
Elliptocyte	/	/	50-200	>200
Hypochromasia	/	/	110-200	>200
Macrocytosis	/	/	110-200	>200
Microcytosis	/	/	110-200	>200
Ovalocyte	/	/	50-200	>200
Poikilocytosis	/	/	/	/
Polychromasie	/	/	50-200	>200
Sickle cell / drepanocyte	/	/	10-20	>20
Stomatocyte	/	/	50-200	>200
Target cell	/	/	50-200	>200
Dimorphism	If present	/	/	/
Pappenheimer bodies	/	/	20-30	>30
Howell-Jolly body	/	/	20-30	>30
Basophilic stippling	/	/	50-200	>200
Teardrop cell/ dacrocute	/	/	50-200	>200
Spherocyte	/	/	50-200	>200
Schistocyte/fragmentocyte	/	<10	10-20	>20
Rouleaux	If present	/	/	/
Agglutination	If present	/	/	/
Parasites	If present	/	/	/

\*All counts per 1000 RBC

# Commentaren



- ▶ Post-analytische fase
  - ▶ Helpt de clinicus in de interpretatie
  - ▶ Verduidelijkt de expertise van de klinisch bioloog
  - ▶ Herinnering van relevante pathologie en investigaties
- ▶ Gebruik aangeraden door
  - ▶ ISO15189
- ▶ Standaardisatie en evaluatie
  - ▶ Bv Harmonization of interpretative comments in laboratory hematology reporting. Recommendations from the Working Group on Diagnostic Hematology of the Italian Society of Clinical Chemistry and Clinical Molecular Biology
  - ▶ EQE

# Commentaren: Voorbeelden

- ▶ 1) Aanwezigheid van acanthocyten 2+, Howell Jolly bodies 2+, Pappenheimer bodies 2+. Argumenten voor hyposplenisme?
- ▶ 2) Leuko-erythroblastaire formule. Aanwezigheid van traancellen 3+. Een hematologisch consult is aangewezen ter exclusie van myelofibrose.
- ▶ 3) Aanwezigheid van grove basofiele stippling 3+. Clinico-anamnestisch argumenten voor lood-intoxicatie? Eventueel aan te vullen met bepaling loodspiegel.

# Verbeteringen workflow AZ Delta - Labo

- Aanpassen graderingssysteem
  - Focus op klinisch relevante aandoeningen
  - Shift naar RBC-Indices
    - Micro/macro => MCV
    - Anisocytose => RDW
    - Poikilocytose => specifieke afwijking
- Toevoegen van commentaren bij significante bevindingen
  - Gericht op specialisatie aanvrager?
  - Gestandaardiseerd?
  - Weergave in Medisch dossier

Suggestie nieuwe graderingstabel AZDelta	Aanwezig	1+	2+	3+
Schistocyte/fragmentocyte	/	1-10	10-20	>20
Sickle cell / drepanocyte	/	1-10	10-20	>20
Teardrop cell/ dacrocute	/	10-50	50-200	>200
Spherocyte	/	10-50	50-200	>200
Acanthocyte	/	/	50-200	>200
Anulocyte	/	/	50-200	>200
Echinocyte	/	/	50-200	>200
Elliptocyte	/	/	50-200	>200
Ovalocyte	/	/	50-200	>200
Polychromasie	/	/	50-200	>200
Stomatocyte	/	/	50-200	>200
Target cell	/	/	50-200	>200
Basophilic stippling	/	/	50-200	>200
Pappenheimer bodies	/	/	20-30	>30
Howell-Jolly body	/	/	20-30	>30
Rouleaux	Aanwezig	/	/	/
Agglutination	Aanwezig	/	/	/
Parasites	Aanwezig	/	/	/
Dimorphism	Aanwezig	/	/	/
All waarden op 1000 RBC's				

# Verbeteringen AZ Delta - Clinici

- ▶ Organiseren ‘opleiding’ van clinici vanuit laboratorium
  - ▶ Continue educatie door aanbieden commentaren
  - ▶ Regeling nieuwe nieuwsbrief met toelichting van een aspect van de RBC-M
  - ▶ Lessen aangeboden op de verscheidene kransen
- ▶ Meer open interactie met laboratorium
  - ▶ Commentaren + kennisgeving expertise
  - ▶ Toegevoegde waarde van KB als consulent

# Voorbeeld nieuwbrief

## ► Structuur

- ▶ Wat wordt er bedoeld met de term?
- ▶ Pathogenese en klinische relevantie?
- ▶ Geassocieerde aandoeningen
  - ▶ Frequentie pathologie
  - ▶ Enkele zeldzame prominente oorzaken

Acanthocytes (ἄκανθα: Thorn/Spine) Synonym: Spur cell.

An acanthocyte is a densely stained erythrocyte with 2-10 irregularly positioned thorny projections of varying length and thickness. Acanthocytes should be differentiated from echinocytes, whose spicules are more uniform. Acanthocytes can be found in a diverse group of inherited or acquired diseases. Their formation is usually associated with changes in the composition of the lipid bilayer that result in an expansion of the outer leaflet. Due to their abnormal morphology, acanthocytes are more vulnerable to trapping, modulation and destruction by the spleen. This vulnerability can result in mild to severe hemolytic anemia. (1-4)

Acanthocytes can be found in large amounts in liver disease, abetalipoproteinemia and neuro-acanthosis syndromes. They can also be found in smaller amounts in a wide variety of pathologies.

### Liver disease

In both obstructive and hepatocellular liver disease there are abnormalities in serum lipoproteins that induce changes in erythrocyte morphology by disturbing the passive exchange of lipids between plasma and erythrocytes. Cholesterol accumulation in the outer leaflet of the membrane bilayer results in an increase of membrane surface area. This superfluous membrane can manifest itself as target cells or acanthocytes. (1-4)

In severe liver disease the combination of acanthocytosis and hemolysis can be indicative of a spur cell anemia. This is an acquired abnormality of the erythrocyte that occurs in a small number of patients with end-stage liver disease. Spur cell anemia is characterized by a rapidly progressive hemolysis as well as excessive amounts of acanthocytes on the peripheral blood smear. It is most commonly seen in alcoholic liver disease, but has been described in patients with other hepatic diseases as well. (5-6)

### Various other common causes

Acanthocytes can also be found, usually in smaller amounts, in the peripheral blood in several other disease states such as malnutrition (e.g. anorexia nervosa, cystic fibrosis), hypothyroidism, diffuse intravascular coagulation, myelodysplasia and splenectomy. Additionally, commonly prescribed drugs (statins, misoprostol) have been associated with the formation of acanthocytes. (7-16)

### Rare congenital causes

#### Abetalipoproteinemia (Bassen-Kornzweig syndrome)

Abetalipoproteinemia is a rare (prevalence < 1/1000000) autosomal recessive disorder caused by a mutation in the gene encoding the microsomal triglyceride transfer protein (MTTP). This defect results in the inability to produce or transport chylomicrons and VLDL. This deficiency impairs uptake in the intestinal mucosa and results in low plasma triglyceride levels and markedly decreased plasma cholesterol and phospholipid levels. An excess of sphingomyelin, preferentially inserting in the outer membrane leaflet, results in an increase of the surface area and subsequently acanthocytosis. (17-18)

#### Neurological syndromes

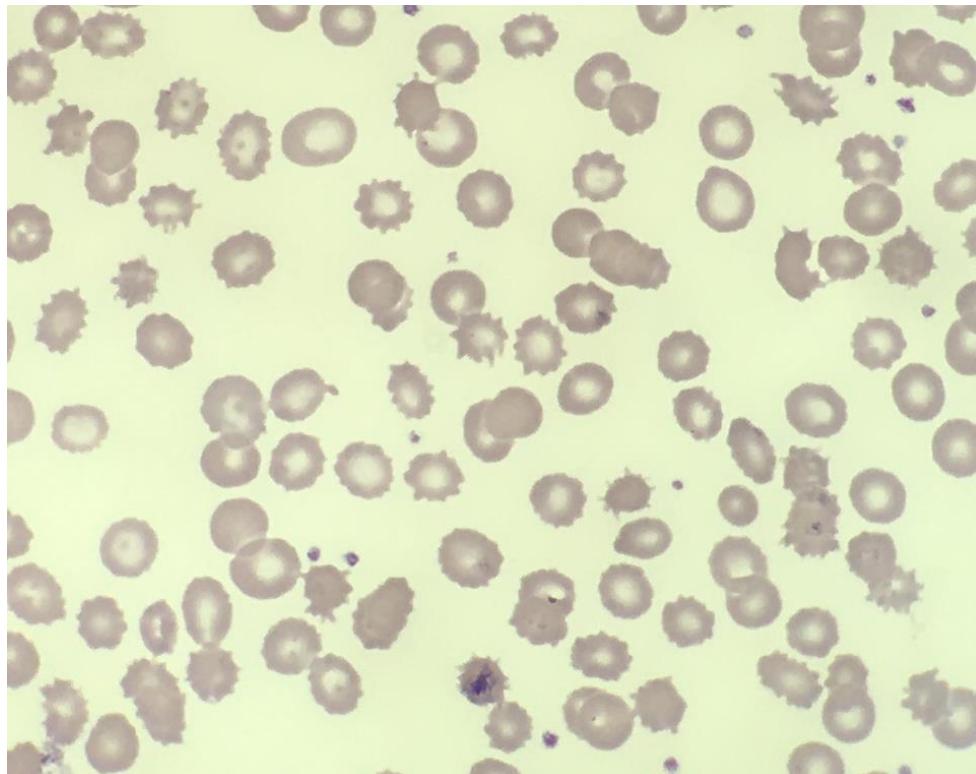
The neuro-acanthocytosis syndromes are a rare (prevalence < 1-5/1000000) group of syndromes characterized by progressive neurodegeneration in adolescent or adult life and the presence of acanthocytes on the blood smear. The mechanisms underlying acanthocyte formation in the neuro-acanthocytosis syndromes are not yet fully understood. (19-20)

# To Do

- ▶ Resultaten survey bespreken met clinici in functie van mogelijke aanpassingen en verwachtingen.
- ▶ Implementeren van aanpassingen zoals hierboven beschreven.
- ▶ Extra: Prospectief onderzoek naar prevalentie van afwijkingen in verschillende populaties voor opstellen evidence-based-grading criteria in plaats van consensus-based.

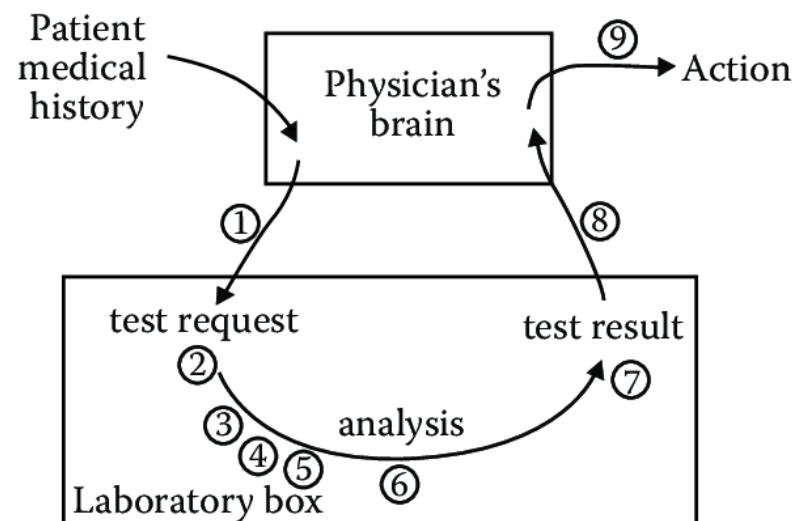
# Algemeen voorbeeld

Een 56-jarige patiënt met gevorderde levercirrose en anemie ondanks meerdere transfusies.



Oud: Aanwezigheid van acanthocyten

Nieuw: Aanwezigheid van acanthocyten 3+.  
DD spur cell anemie? Eventueel aan te vullen met directe coombs.

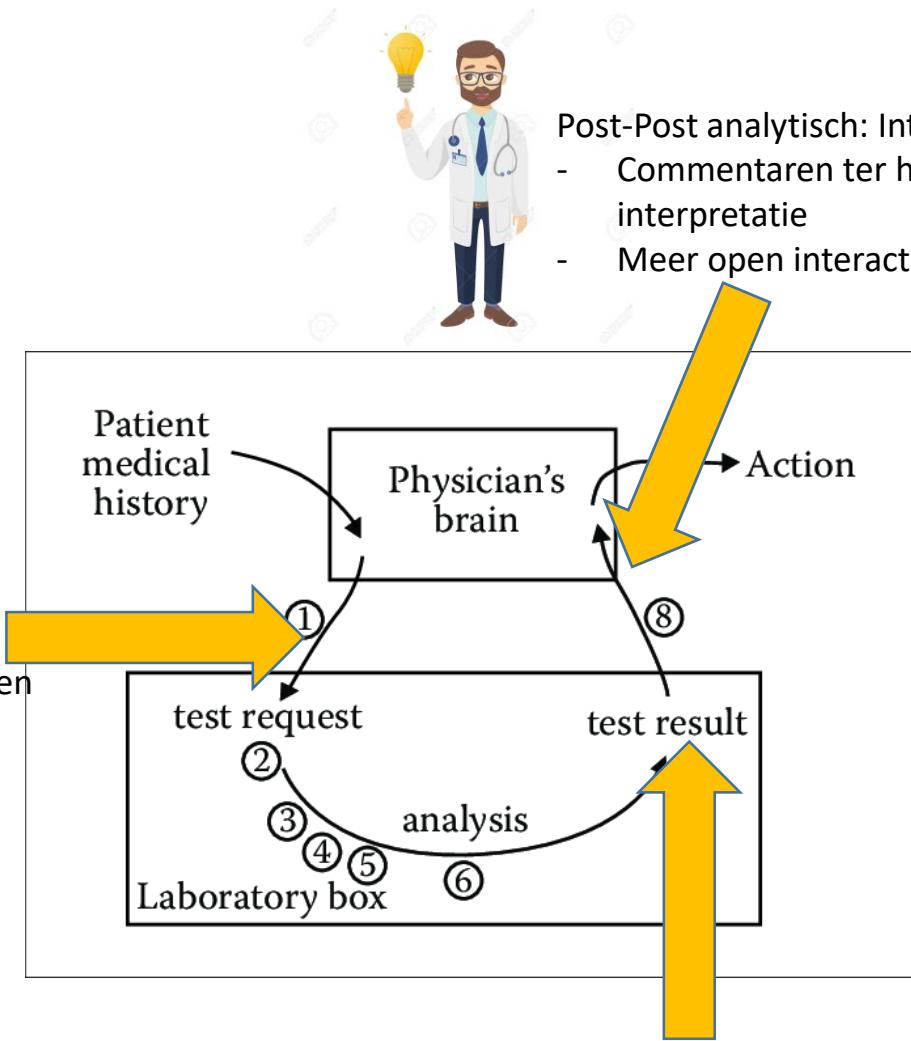


#### Pre-analytisch: Awareness

- Nieuwbrief
- Opleiding via commentaren

Post-Post analytisch: Interpretatie

- Commentaren ter hulp in interpretatie
- Meer open interactie



#### Post-analytisch: Rapportering

- Aanpassing gradering
- Meer klinisch relevante data

**Bedankt!**