SIMeL
SOCIETÀ ITALIANA
MEDICINA DI LABORATORIO

Milano 11 novembre 2010

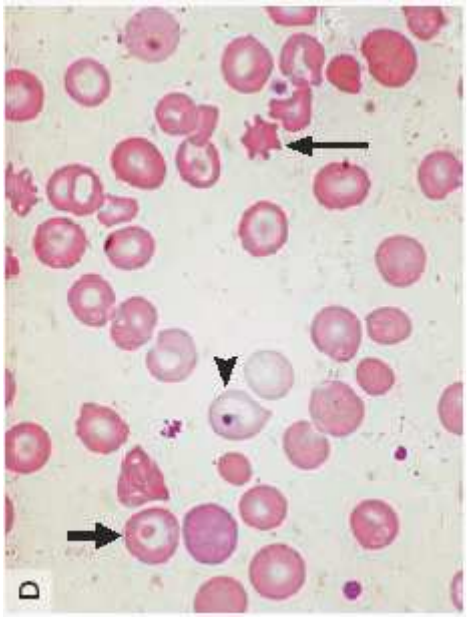
Ematologia di Laboratorio

Paolo Doretto

Piero Cappelletti

Diagnosis from the Blood Smear

- Even in the age of molecular analysis, the blood smear remains an important diagnostic tool.
- Physicians should request a blood smear when there are clinical indications for it.
- Members of the laboratory staff should make and examine a blood smear whenever the results of the complete blood count indicate that a blood smear is essential for the validation or the further elucidation of a detected abnormality.



- If error is to be avoided, sophisticated modern investigations of hematologic disorders should be interpreted in the light of peripheral-blood features as well as the clinical context.

B Bain 2005

White Blood Cell Morphology in the Balance

Like many in the hematology laboratory profession, I have spent countless hours reading blood films, bone marrows, and body fluids. But did I ever *seriously* ask if I was making an impact on medical decisionmaking with my morphology assessments?

B Houwen 2005

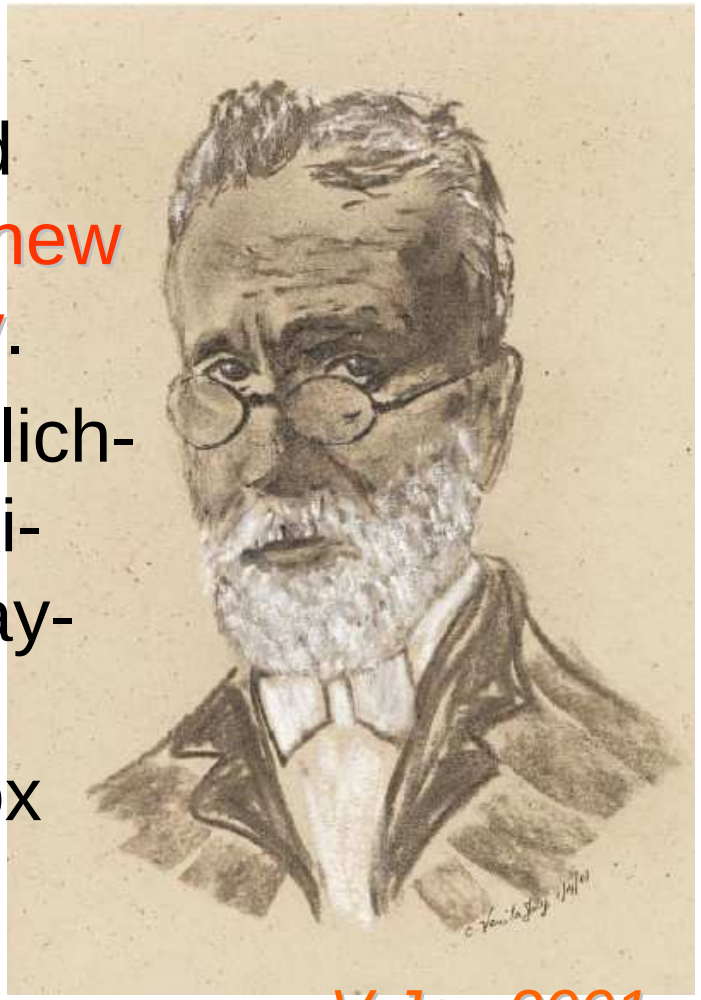
Esiste e cos'è l'ematologia di laboratorio?

- Ematologia di Laboratorio
  - disciplina morfologica
  - disciplina tecnologica
  - disciplina clinica

- Logica diagnostica dell'ematologia di laboratorio

Ematologia di Laboratorio: una disciplina morfologica

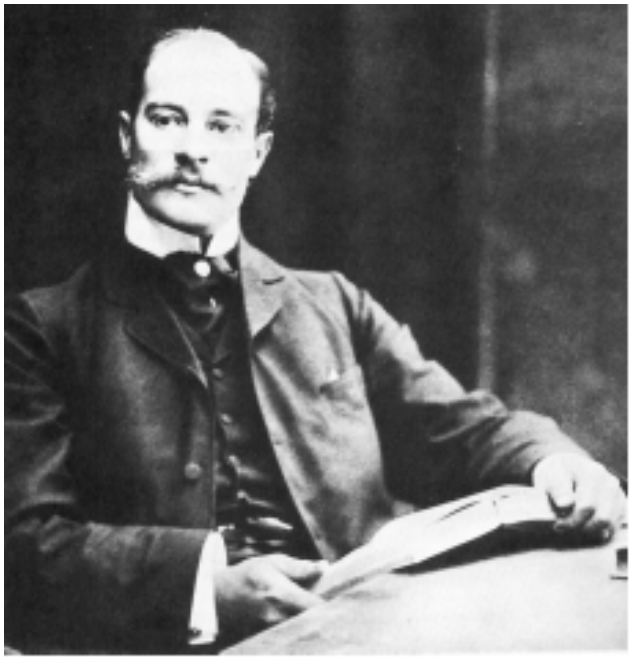
- Ehrlich's staining of blood films ("triacid": methylene green, acid fuchsin, orange G) launched a new era in the history of hematology.
- Woronzoff-Dashkoff K: The Ehrlich-Chenzinsky-Plehn-Malachowski-Romanowsky-Nocht-Jenner-May-Grunwald-Leishman-Reuter-Wright-Giemsa-Lillie-Roe-Wilcox Stain: The mystery unfolds. Clin Lab Med 1993;13:759



V Jay 2001

Morphologische Hematologie

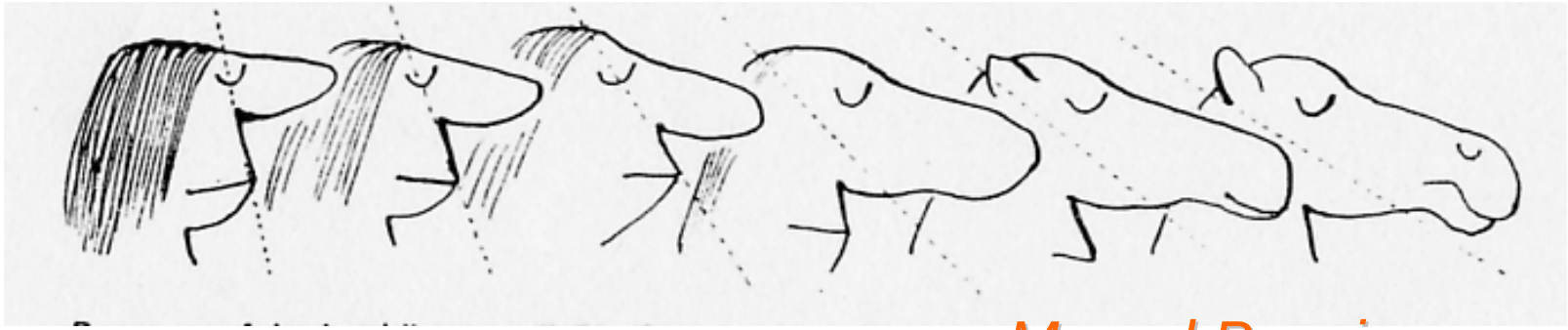
Artur Pappenheim



- He used dried smears stained with Romanowsky's stains and recognized that blood formation is a dynamic process stemming from the marrow.
- On the basis of morphology alone he claimed that he could trace all the cells of the blood to a common ancestral cell the *Lymphoidozyt*.
- He was the author of a textbook on morphology (Morphologische Haematologie) and the editor of an hematology journal (Folia Haematologica).

Il legame forma-funzione

- Les cellules sur frottis pour ce qu'elles sont: des cadavres aplatis et brillamment colorés. Ces choses motes ont eu une vie intense. C'est cette vie, c'est l'histoire naturelle des cellules du sang, que …s'efforce de reconstituer
- Une *belle* image éclaire ce que l'on savait confusement, exite l'imagination et se fixe ppur tojours dans la memoire, avec ses vertus d'explication et de suggestion.



Marcel Bessis

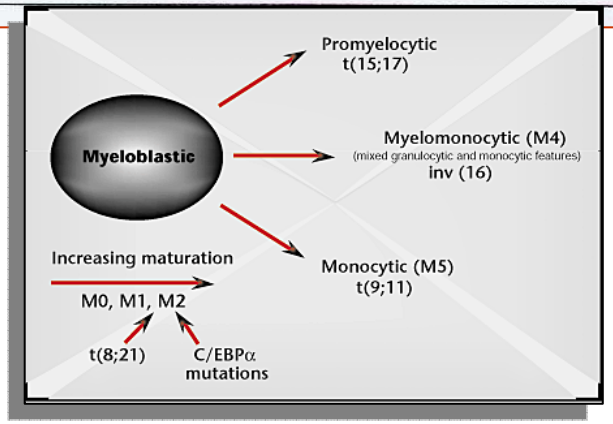
La storia della leucemia

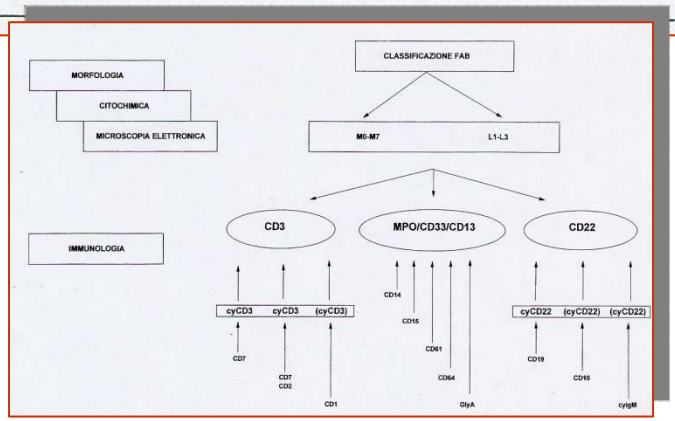
- Virchow, R. (1856) Die Leukämie. In: *Gesammelte Abhandlungen Zur Wissenschaftlichen Medizin*, pp. 190-211. Meidinger, Frankfurt.
- “It is moreover, the same conclusion which Bennett came to in the much-discussed matter of priority between us when he observed a case of indubitable leukaemia, some months before I saw my first case” *R. Virchow 1858*

French-American-British classification

JM Bennet et al 1976, 1985…

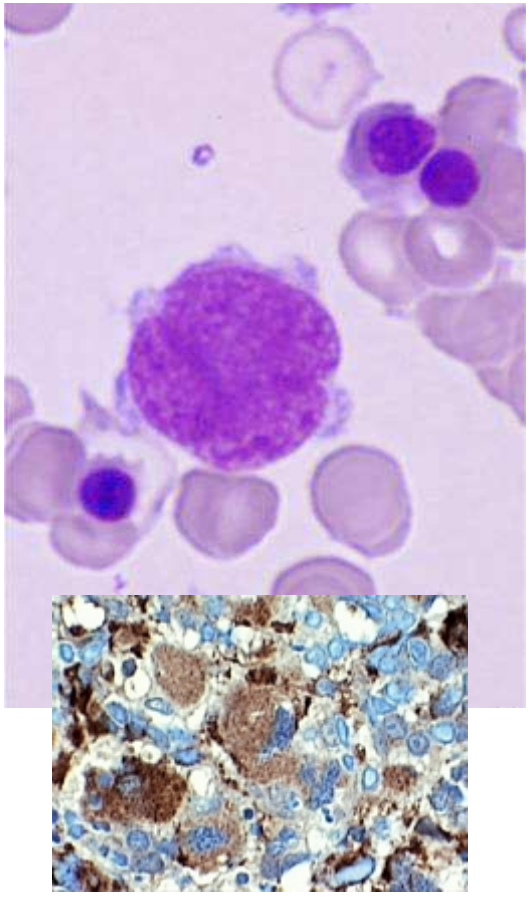
	% DI CELLULE NON ERITROIDI MIDOLLARI		
	BLASTI	COMPONENTE GRANULOCITARIA*	COMPONENTE MONOCITARIA**
M1	>90 % (>3 % MPO+)	< 10%	< 10%
M2	30-89 %	> 10%	< 20 %
M3	~ 30 %	promielociti ipergranulari corpi di Auer	
M3v	nucleo indentato	tipici promielociti ipergranulari meno frequenti	
M4	>30 %	> 20%	> 20 %
M4 eos		con prominente anomala maturazione eosinofila	
M5a	> 30 %	< 20%	> 80% (monoblasti)
M5b	> 30 %	< 20%	> 80% (monociti/blasti)
M6***	> 30%	eritroblasti > 50% degli elementi midollari nucleati	
M7	> 30%	PPO+ (ultrastruttura) + analisi immunologica	





FAB M7: Acute Megakarioblastic Leukemia – Beyond Morphology

- The criteria for M7 represent a significant departure for the FAB group in that ultrastructural cytochemistry or immunologic techniques, or both, are now required to make the diagnosis
- …are we ready for a totally new classification based primarly on cytogenetic or immunologic characterization…?



CD Bloomfield, RD Brunning 1985

EGIL proposals

B lineage ALL	CD19 / CD79a / CD22
Pro-B-ALL	No other differentiation B-cell ag
Common ALL	CD10
Pre-B ALL	Cytoplasmic IgM
Mature B ALL	Cytoplasmic or surface κ λ
T lineage ALL	**Cytoplasmic/membrane CD3**
Pro-T ALL	CD7
Pre-T ALL	CD2 / CD5 / CD8
Cortical –T ALL	CD1a
Mature-T ALL	Membrane CD3, CD1a -
α/β T ALL	Anti-TCR α/β
Γ/δ T ALL	Anti-TCR γ/δ
My + ALL	
Myelomonocitic l.	MPO, CD13, CD33
Erythroid lineage	Glycophorin A
Megakaryocytic l.	CD11 &/or CD61
Early myeloid (M0)	Neg cytochem. & Ly
TdT+ AML	
Ly+ AML	

- Within the major types (B and T cell lineage) of ALL, several groups are delineated according to the degree of cell differentiation.
- Within the AML, only 3 subtypes as defined by the FAB classification (M0, M6, M7) can be unequivocally defined by immunological markers

MC Bene et al 1995

TheWorld Health Organization (WHO) classification of the myeloid neoplasms

- A basic principle of the WHO system is that the classification of hematopoietic and lymphoid neoplasms should utilize not only morphologic findings but also all available information, including genetic, immunophenotypic, biologic, and clinical features to define specific disease entities.
- *3 (+1) subgroups of AML are recognized by the WHO classification: (1) AML with recurrent genetic abnormalities, (2) AML with multilineage dysplasia, and 3) AML and MDS, therapy related, (4) AML, not otherwise categorized.*
- *the blast threshold for the diagnosis of AML from 30% to 20% blasts in the blood or marrow.*
- *patients with the clonal, recurring cytogenetic abnormalities t(8;21)(q22;q22), inv(16)(p13q22) or t(16;16)(p13;q22), and t(15;17)(q22;q12) = AML regardless of the blast percentage*

TheWorld Health Organization (WHO) classification of the myeloid neoplasms

- *In the WHO system, patients with blood or bone marrow specimens that show at least 20% blasts are considered AML, thus eliminating the FAB category RAEBT.*
- *The WHO classification refines the definition of RA and RARS and introduces a new category, RCMD (RCMD-RS)*
- *RAEB is divided into 2 subgroups, RAEB-1 and RAEB-2, depending on the number of blasts in the blood and bone marrow*
- *One myelodysplastic syndrome is defined by a specific cytogenetic abnormality, the 5q- syndrome.*
- *CMML is eliminated from the MDS category and placed in a group of myeloid disorders with features of both myelodysplasia and myeloproliferative diseases, MDS/MPD*

JW Vardiman et al 2002

TheWorld Health Organization (WHO) classification of the myeloid neoplasms

- The blast percentage and assessment of degree of maturation and dysplastic abnormalities in the neoplastic cells should be determined, if possible, from a 200-cell leukocyte differential performed on a peripheral blood smear and a 500-cell differential performed on marrow aspirate smears stained with Wright Giemsa or May-Grünwald Giemsa. The blast percentage should be correlated with an estimate of the blast count from the marrow biopsy section.

JW Vardiman et al 2002

TheWorld Health Organization (WHO) classification of the myeloid neoplasms

- "blast equivalents" = myeloblasts, monoblasts and promonocytes in acute monoblastic/monocytic and acute and chronic myelomonocytic leukemia and the megakaryoblasts in acute megakaryoblastic leukemia
- the abnormal promyelocyte, in acute promyelocytic leukemia (APL)
- Erythroid precursors (erythroblasts) are not included in the blast count except in the rare instance of "pure" erythroleukemia.
- Dysplastic micromegakaryocytes are also excluded
- the percentage of CD34+ cells should not be considered a substitute for a blast count from the smears or an estimate from the bone marrow biopsy. Although CD34 hematopoietic cells generally are blasts, not all blasts express CD34.

JW Vardiman et al 2002

Realistic Pathologic Classification of Acute Myeloid Leukemias

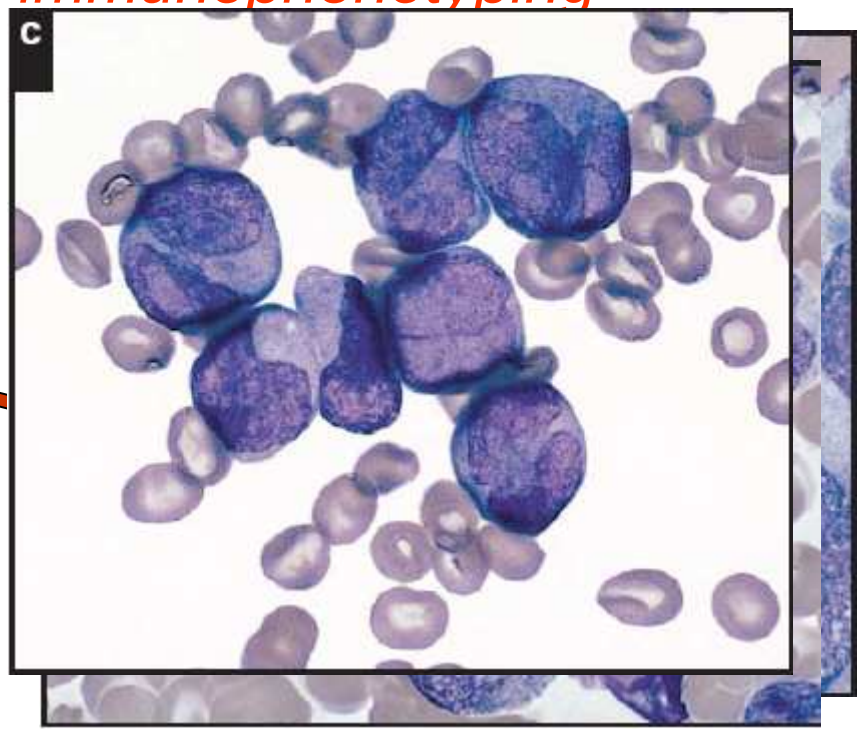
Realistic Pathologic Classification of Acute Myeloid Leukemia

Acute myeloid leukemia, de novo
- Acute myeloid leukemia (with or without monocytic features), not otherwise specified
- Acute myeloid leukemia with changes suggestive of t(8;21)(q22;q22)
  - CD56+
  - CD56–
- Acute promyelocytic leukemia
  - Variant: acute promyelocytic leukemia with features suggestive of t(11;17)(q23;q21)
- Acute myeloid leukemia with abnormal eosinophils suggestive of inv(16)(p13q22) or t(16;16)(p13;q11)
- Acute megakaryoblastic leukemia

Acute myeloid leukemia, myelodysplasia-associated
- Acute myeloid leukemia, treatment-related
- Acute myeloid leukemia arising from myelodysplasia
- Acute myeloid leukemia with associated myelodysplasia

DA Arber 2001

- *diseases correlated with specific cytogenetic translocations and recognized by morphologic evaluation and immunophenotyping*



Integrazione dei dati

...a realistic pathologic classification AMLs that would contain disease types that can be recognized by a combination of morphologic, cytochemical, and immunophenotyping studies.

DA Arber 2001

- From our experience, we suggest that together with morphologic and cytochemical examination, a panel of mAbs against MPO, cyCD3, cyCD79a, CD13, CD33, CD10, CD19, CD2, and CD117 might be a cost-effective, highly predictive screening tool to predict lineage differentiation of acute leukemias.

Thalhammer-Scherrer et al 2002

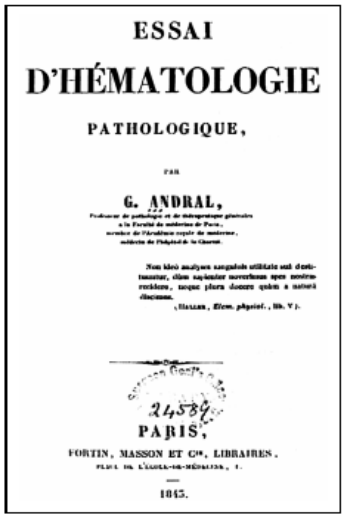
Novità classificazione WHO 2008 delle neoplasie mieloidi

- Incorporazione formale delle anomalie genetiche (traslocazioni cromosomiche e mutazioni geniche) nell'algoritmo diagnostico per la diagnosi di AML
  - *t*(6;9)(p22;q23), *inv*(3)(p21;q26.2) o *t*(3;3)(p22;q23), *t*(1;22)(p13;q13), con mutazione *NPM1, CEBPA*
  - Leucemie acute di lineage ambiguo
  - Proliferazioni mieloidi correlate a sindrome di Down
  - Neoplasia a cellule dendritiche blastiche plasmacitoidi
- Da integrare con i dati clinici, morfologici e/o immunofenotipici

Novità classificazione WHO 2008 delle neoplasie mieloidi

- Citopenia refrattaria con displasia unilineare o multilineare (CRDM) con o senza sideroblasti ad anello
- Sindrome mielodisplastica del bambino
- Sindrome mielodisplastica non classificabile
- Casi con corpi di Auer e blasti <5% SP e <10% MO vanno classificati come AREB 2
- Percentuale di cellule displastiche considerata significativa per la diagnosi è il 10% per la linea eritroide e granulocitaria
- Displasia megacariocitaria significativa: 10% di MKC contando almeno 30 MKC

Ematologia di Laboratorio: una disciplina tecnologica


ESSAI

D'HÉMATOLOGIE

PATHOLOGIQUE,

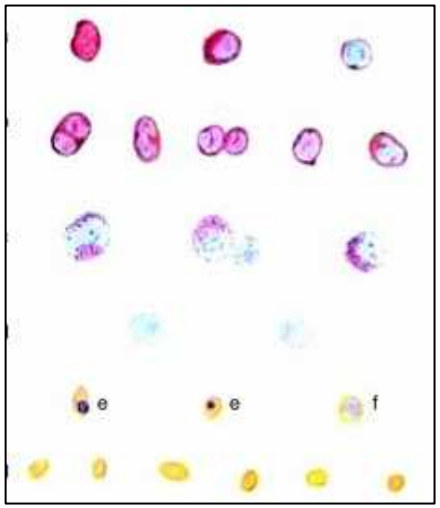
G. ANDRAL,

24589

PARIS,

FORTIN, MASSON ET Cie, LIBRAIRES.

1845.



Blood pure and eloquent:
a story of discovery, of people, and of ideas

The early beginnings

Introduction of quantitation

The morphologic era of hematology

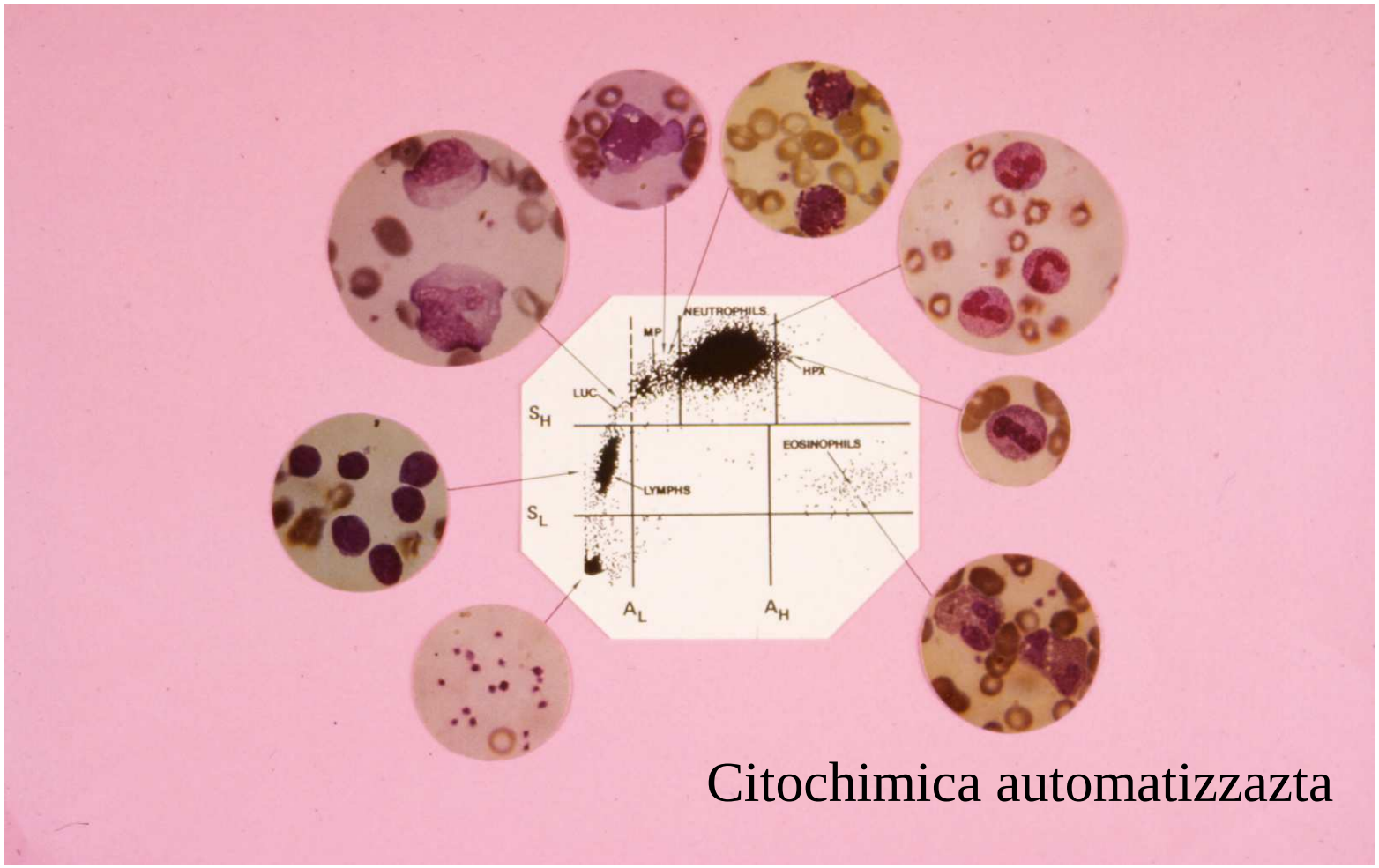
The physiologic revolution

The technologic revolution

M.M. Wintrobe 1976

In principio fu Coulter

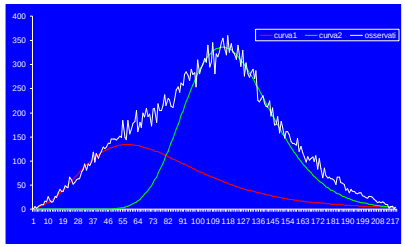
Riconoscimento cellulare

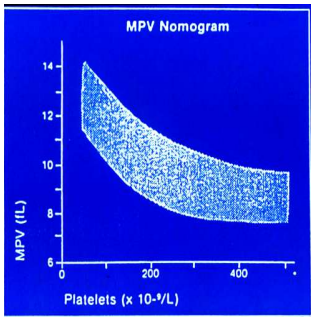


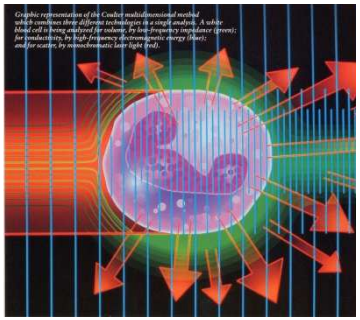
Citochimica automatizzazta

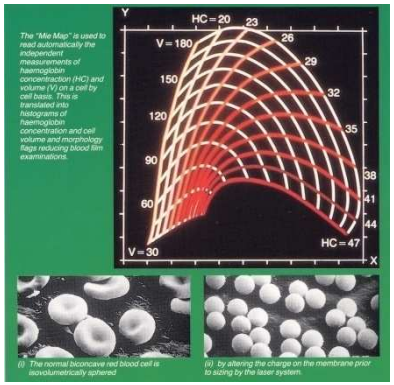
Misure e metodi

1. Ampiezza della distribuzione dei volumi eritrocitari (RDW)
2. Indici piastrinici
3. Superamento dello shape factor
4. Sincretismo tecnologico

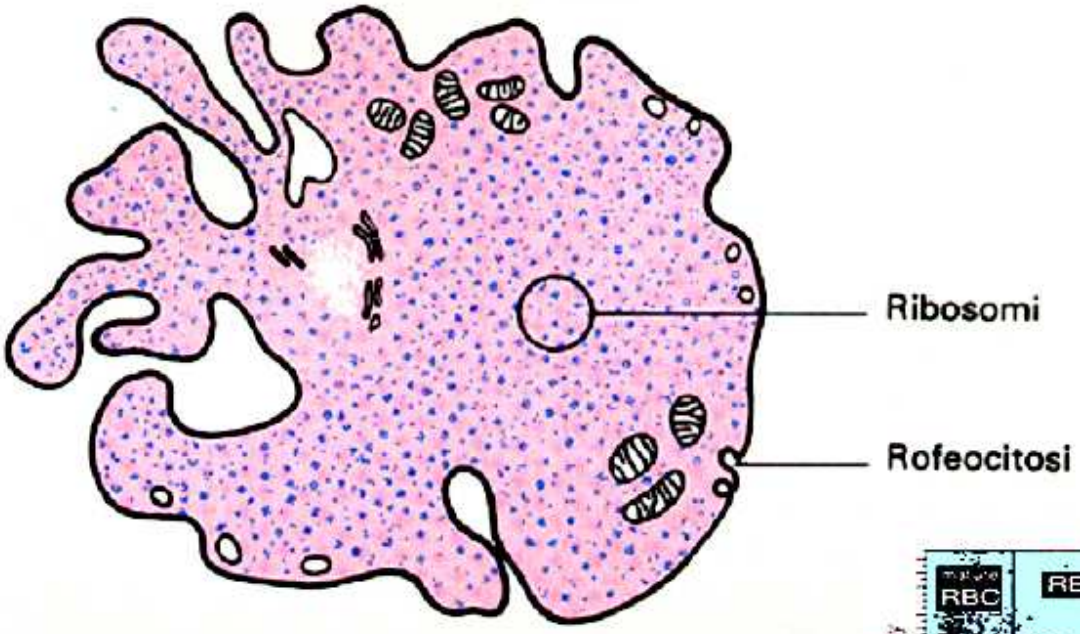


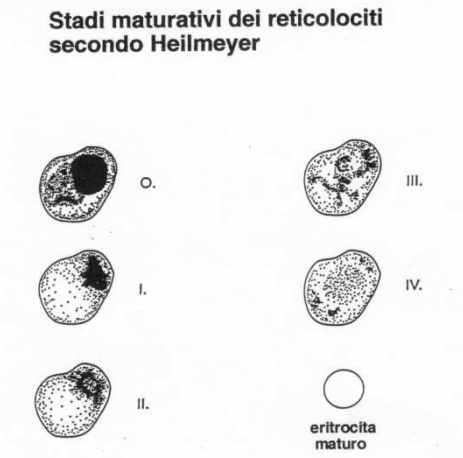


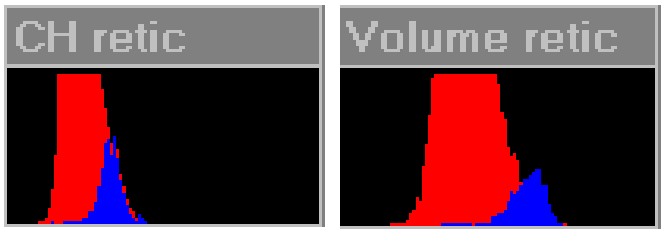


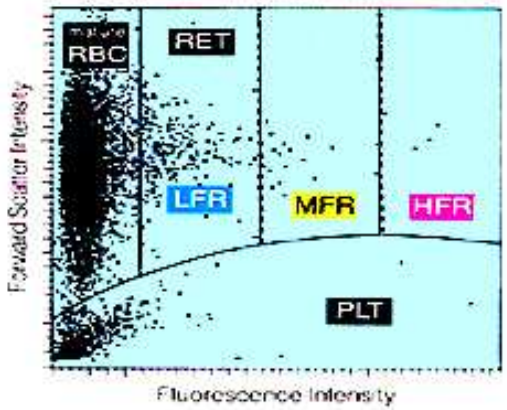


Nuovi riconoscimenti cellulari: i reticolociti





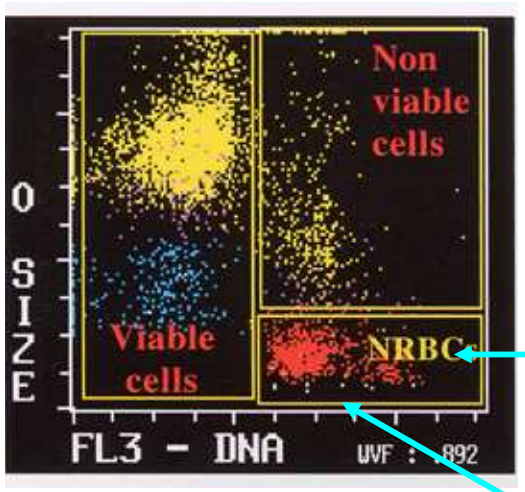


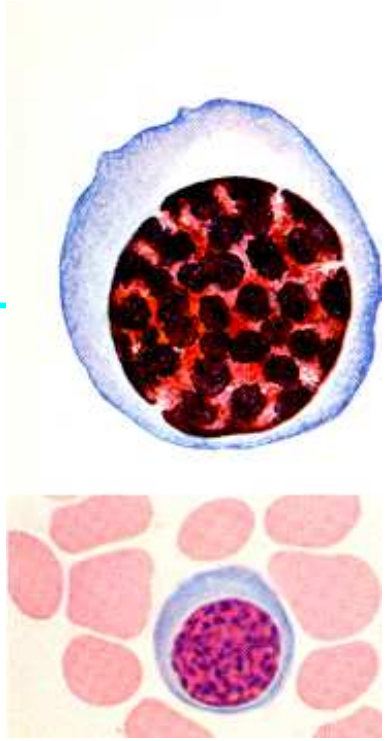


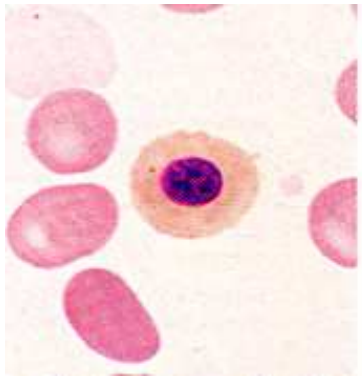
L'area dei reticolociti viene suddivisa in tre parti uguali: il numero di cellule presenti in ciascuna di queste è calcolato e riportato come percentuale riferita al numero totale dei reticolociti.

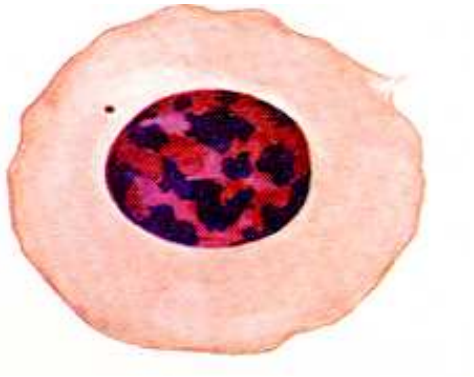
LFR : Low Fluorescence Ratio
MFR : Middle Fluorescence Ratio
HFR : High Fluorescence Ratio

Nuovi riconoscimenti cellulari: gli eritroblasti

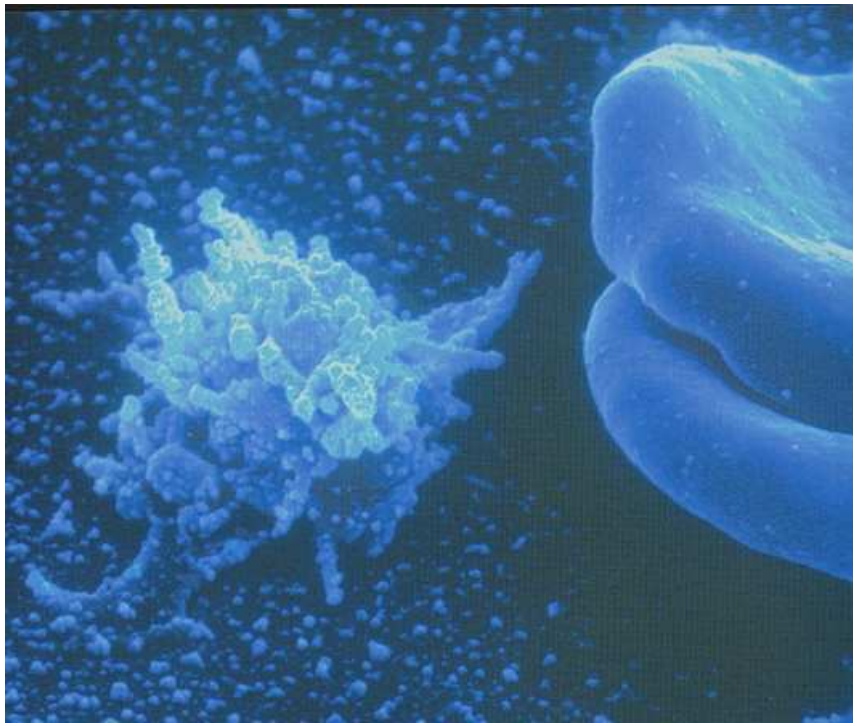


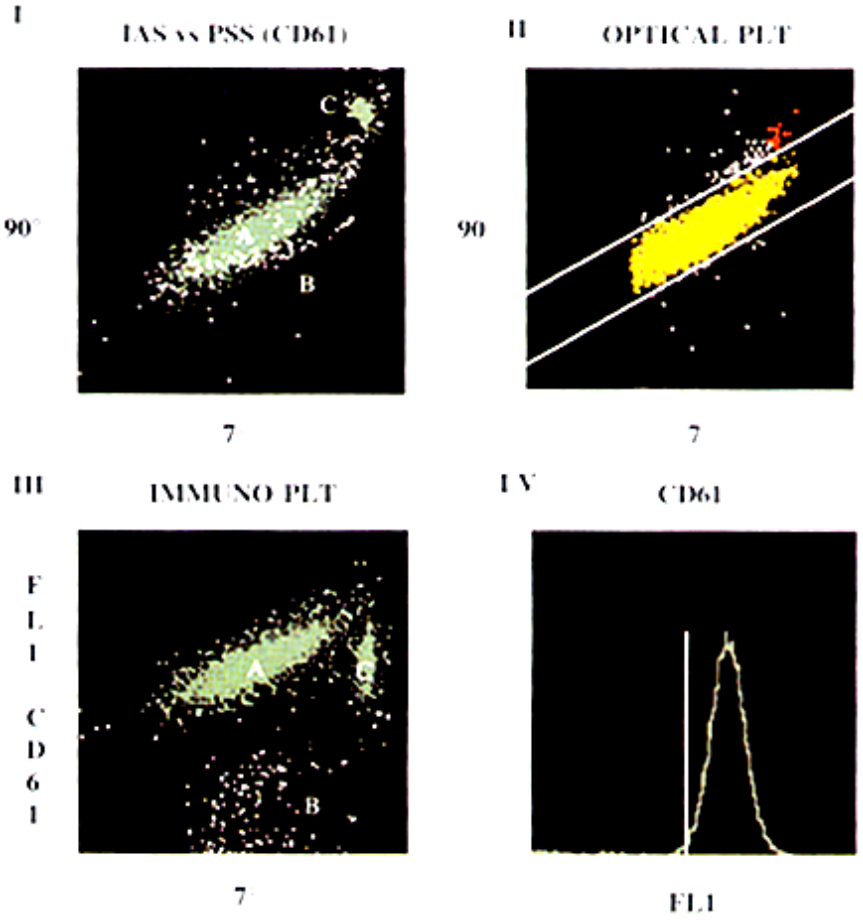






Nuovi riconoscimenti cellulari: piastrine con CD 61

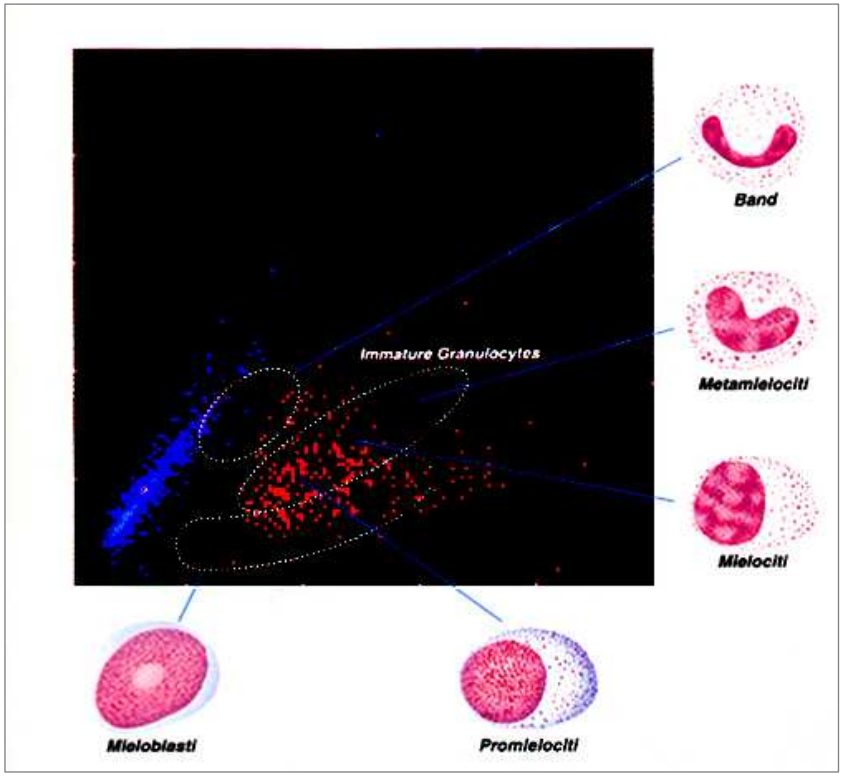


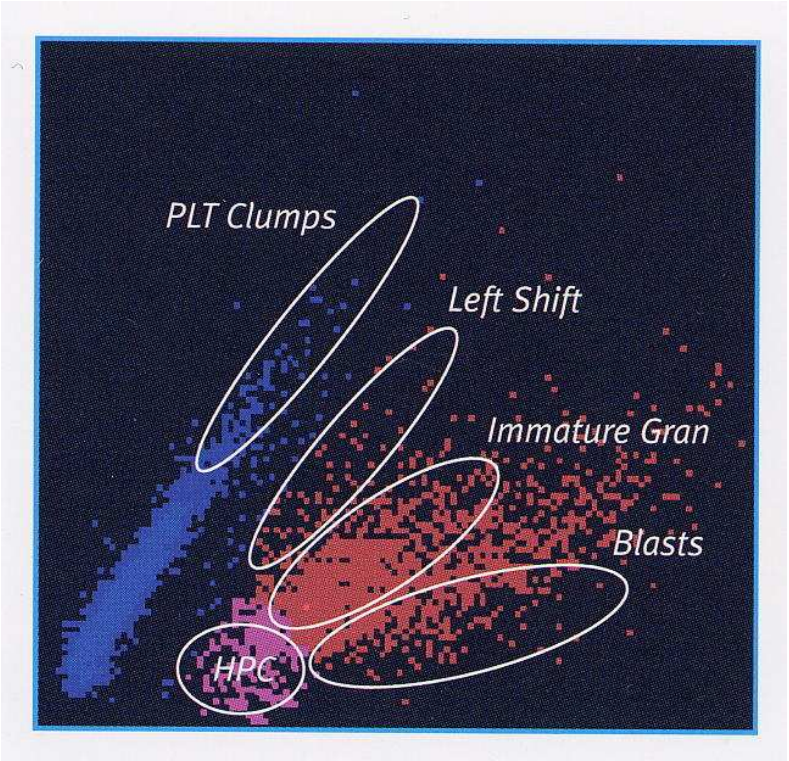


10	x10⁹/L	CV%	13.9
20	x10⁹/L	CV%	8.0

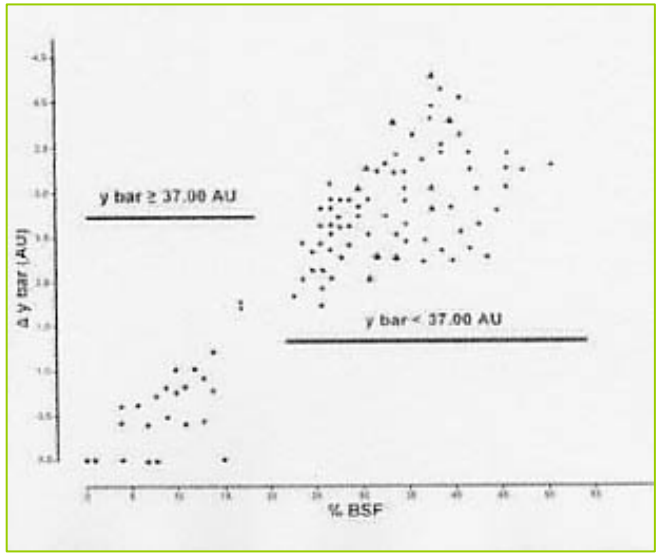
Ault 1996

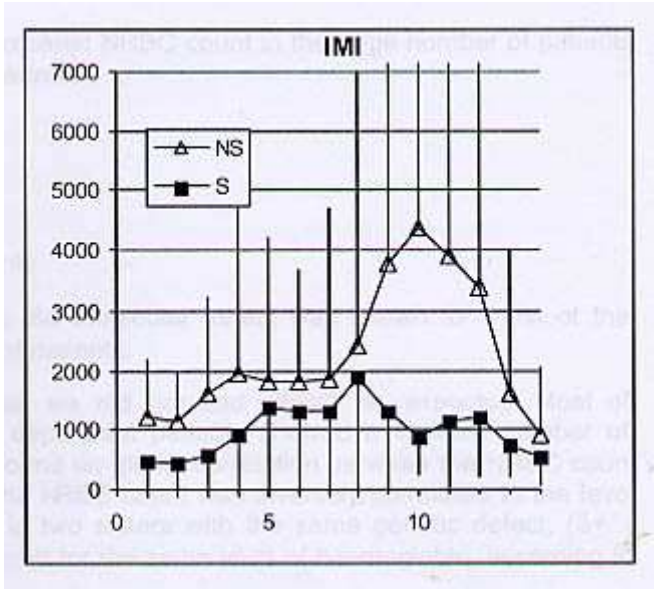
Nuovi segnali cellulari: immaturità e precursori

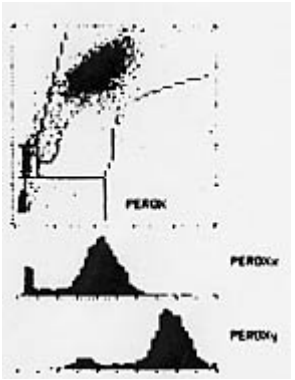




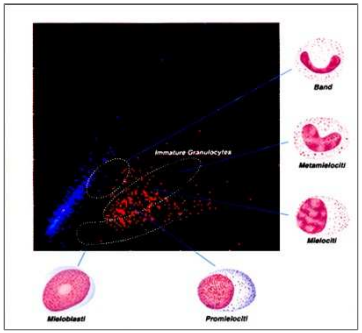
Nuovi segnali cellulari: attivazione neutrofili







Lippi et al 1993



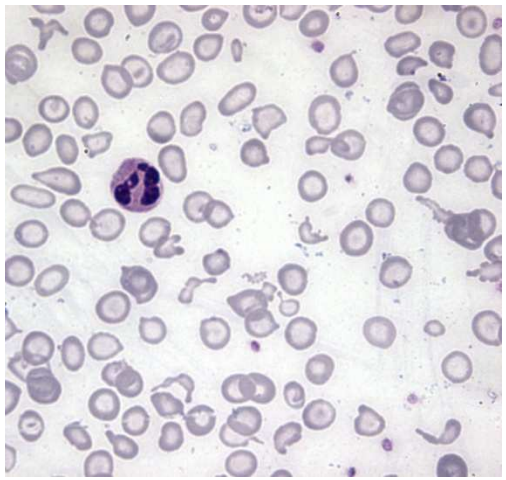
Nierhaus A 2003

Nuovi segnali cellulari: schistociti

Table 2
Sensitivity and Specificity and Negative and Positive Predictive Values at Different Thresholds*

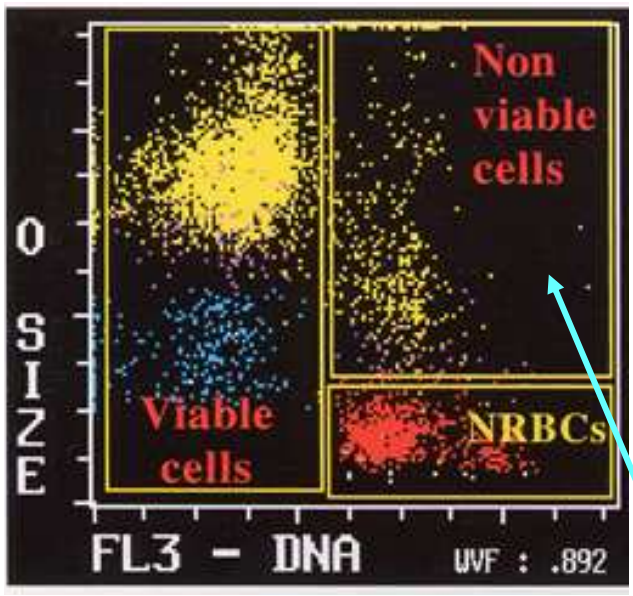
	Threshold (Schistocytes, %)	Sensitivity (%)	Specificity (%)	Predictive Value	
				Positive	Negative
ADVIA 120	0.25	100	17.1	23.0	100
	1.0	88.5	87.6	63.9	96.8
Microscope	0.2	100	66.7	42.6	100
	0.5	96.2	93.3	78.1	98.9

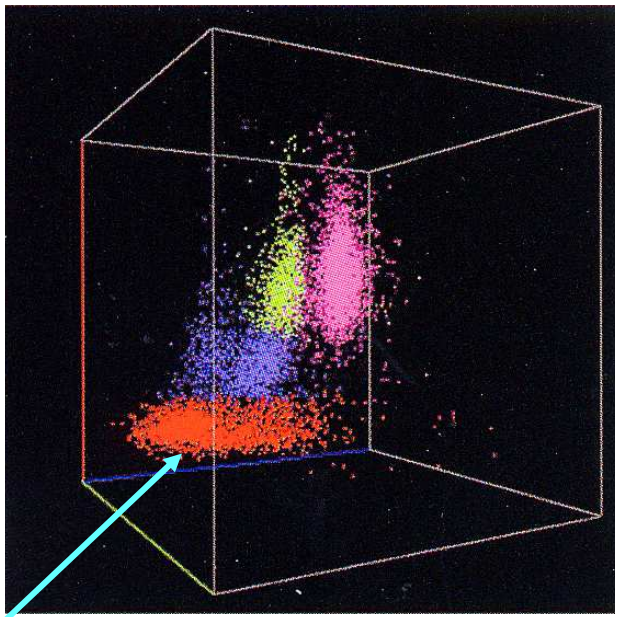
* Percentages of automated RBC fragments and schistocytes evaluated under the microscope. For proprietary information, see the text.

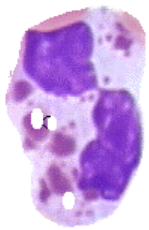


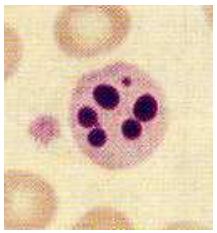
JF Lesesve et al 2004

Nuovi segnali cellulari: funzionalità cellulare









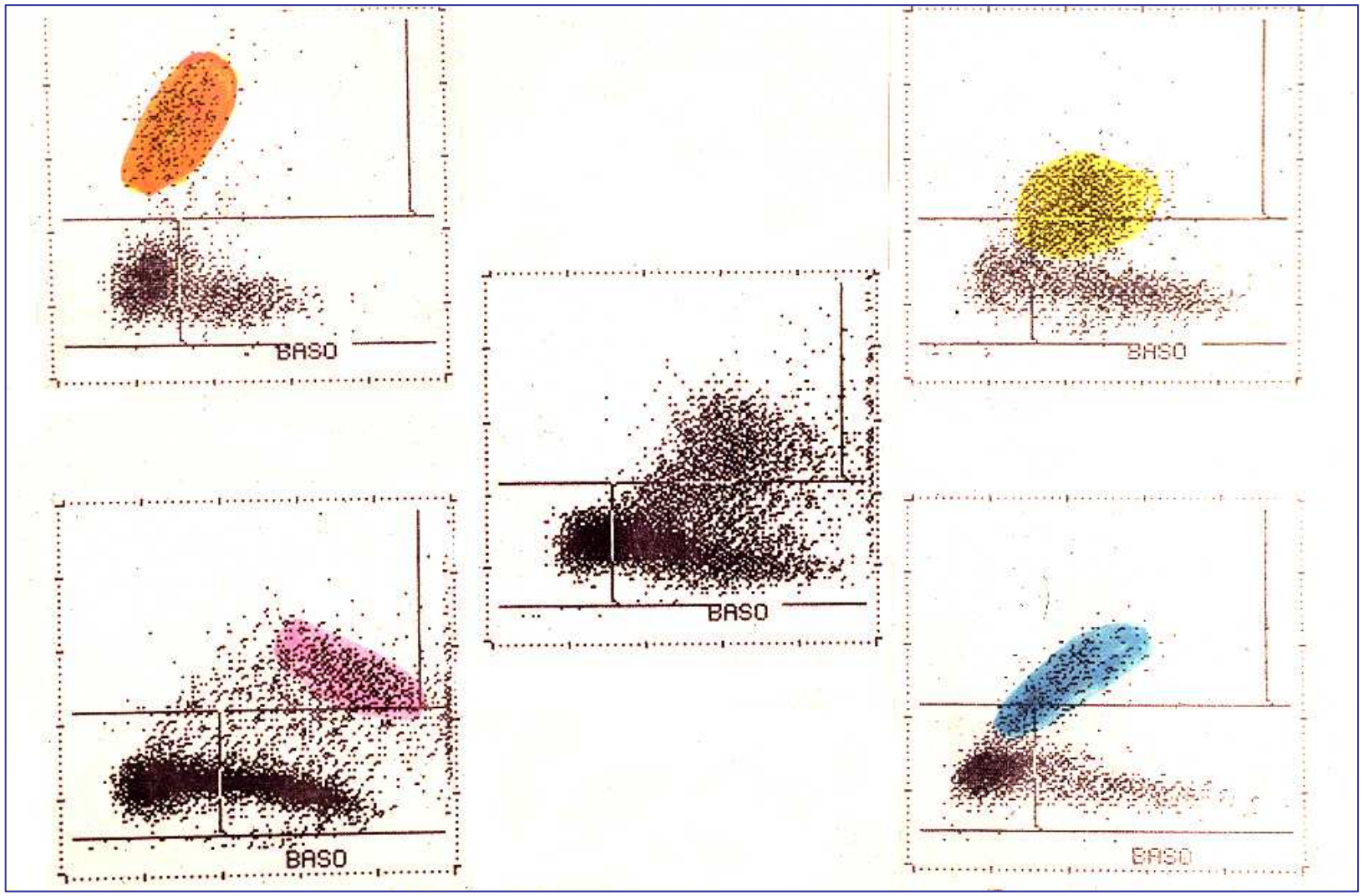
apoptosi

E Piva 2002

Morfologia strumentale

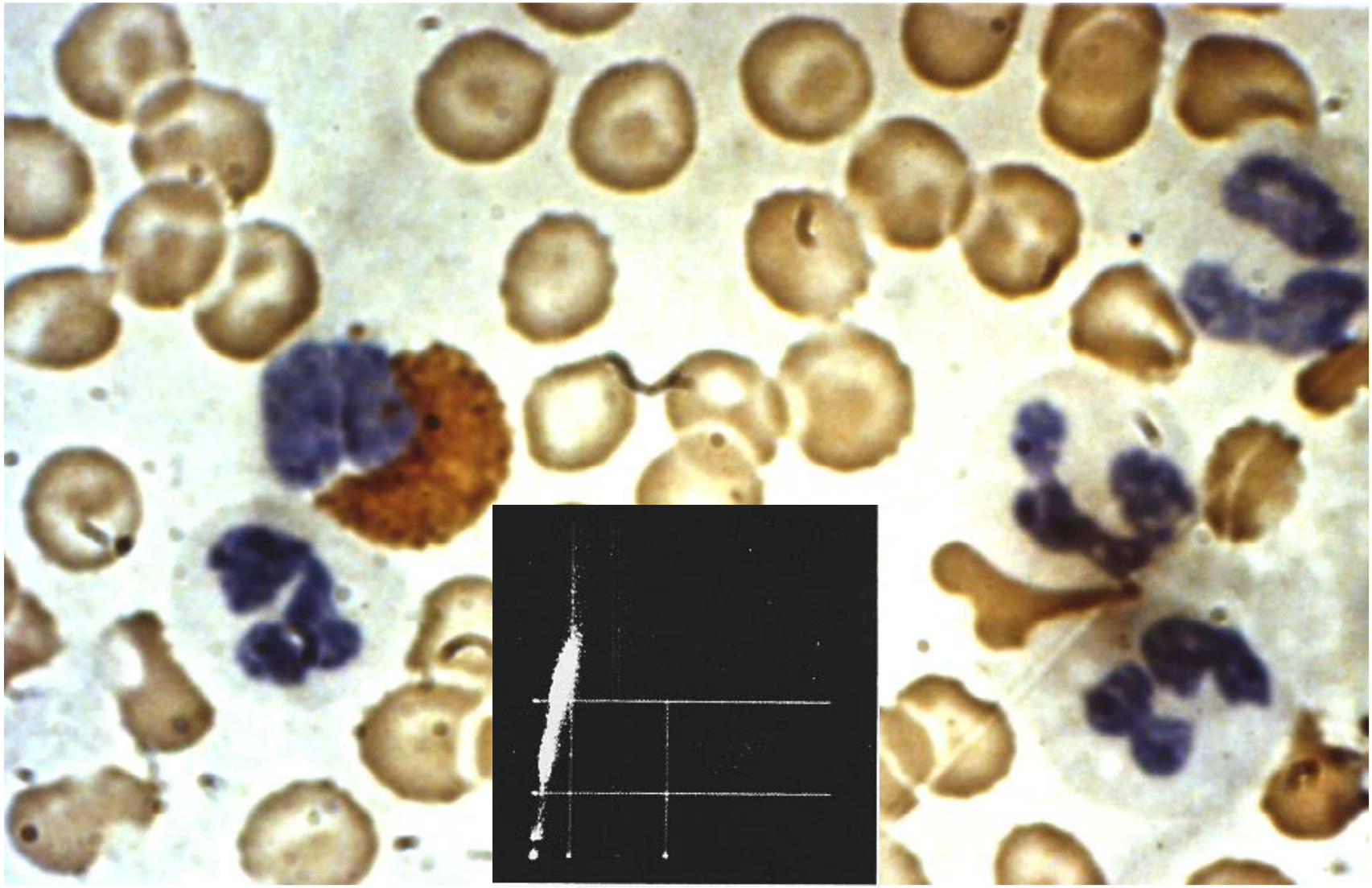
- “morfologia strumentale” come insieme dei dati numerici, allarmi, istogrammi e citogrammi degli strumenti che l’occhio clinico compone secondo pattern dai correlati morfologici
- il compito del medico di laboratorio: integrare i dati strumentali e morfologici, per i dovuti approfondimenti diagnostici, e segnalare i suggerimenti interpretativi, utilizzando al meglio le notizie cliniche, quando disponibili.

Pitfalls and pseudopitfalls



P Cappelletti et al 1989

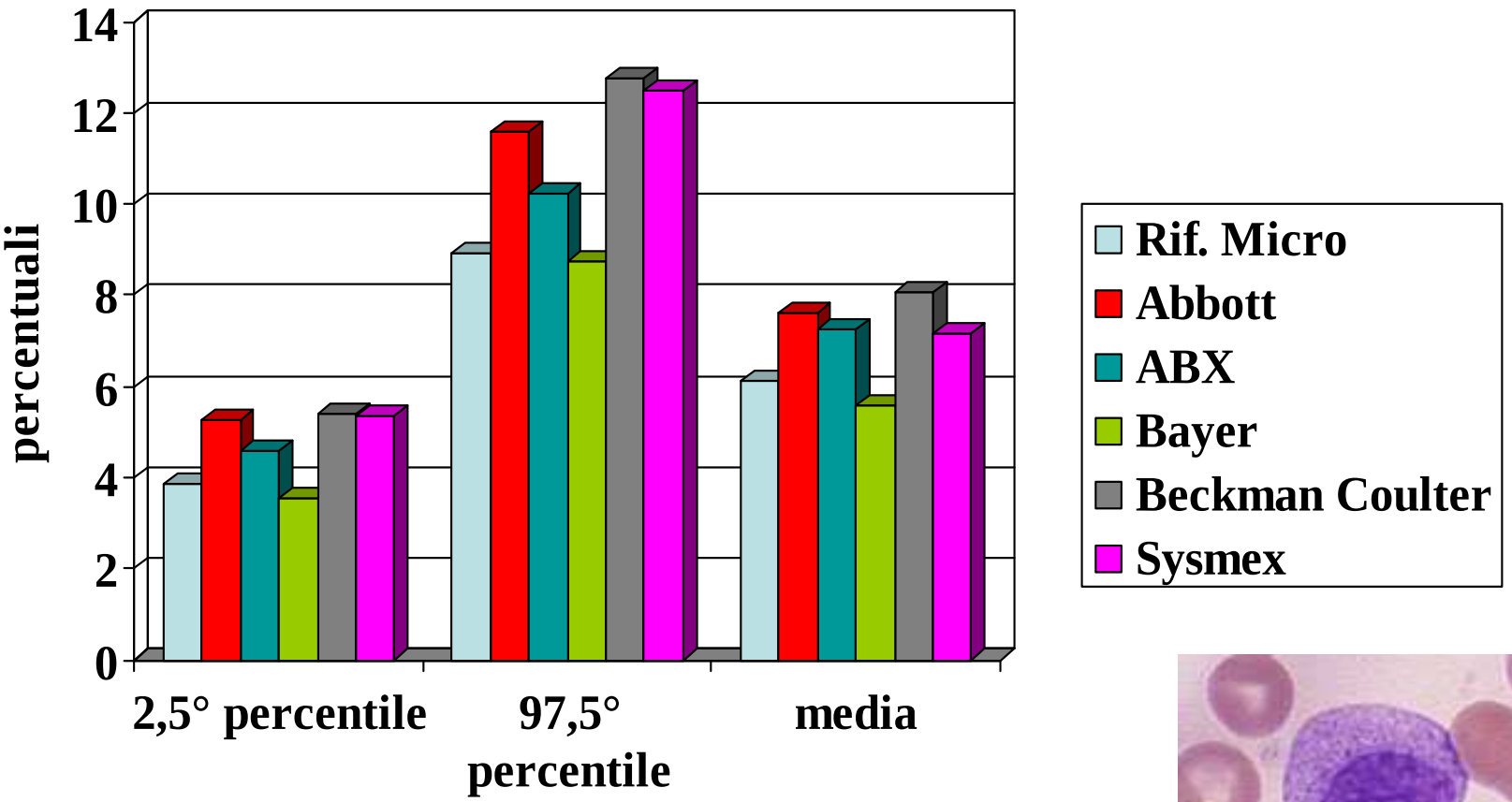
Hematology beyond microscopy

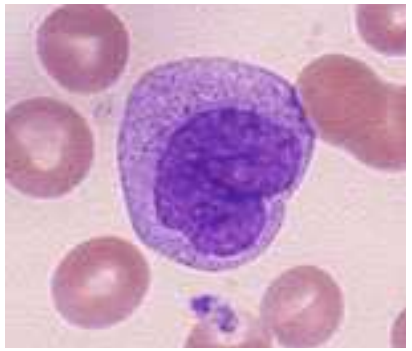


Hematology beyond microscopy

- Il problema del riferimento
  - CLSI H-20 A
  - Plts: CD41 – CD61
- L'obiettivo clinico
  - Screening dei patologici
  - Una nuova "formula"

Intervalli di riferimento monociti %





GdS-E SIMeL 2003

Evaluation of the monocyte counting by two automated haematology analysers compared with flow cytometry

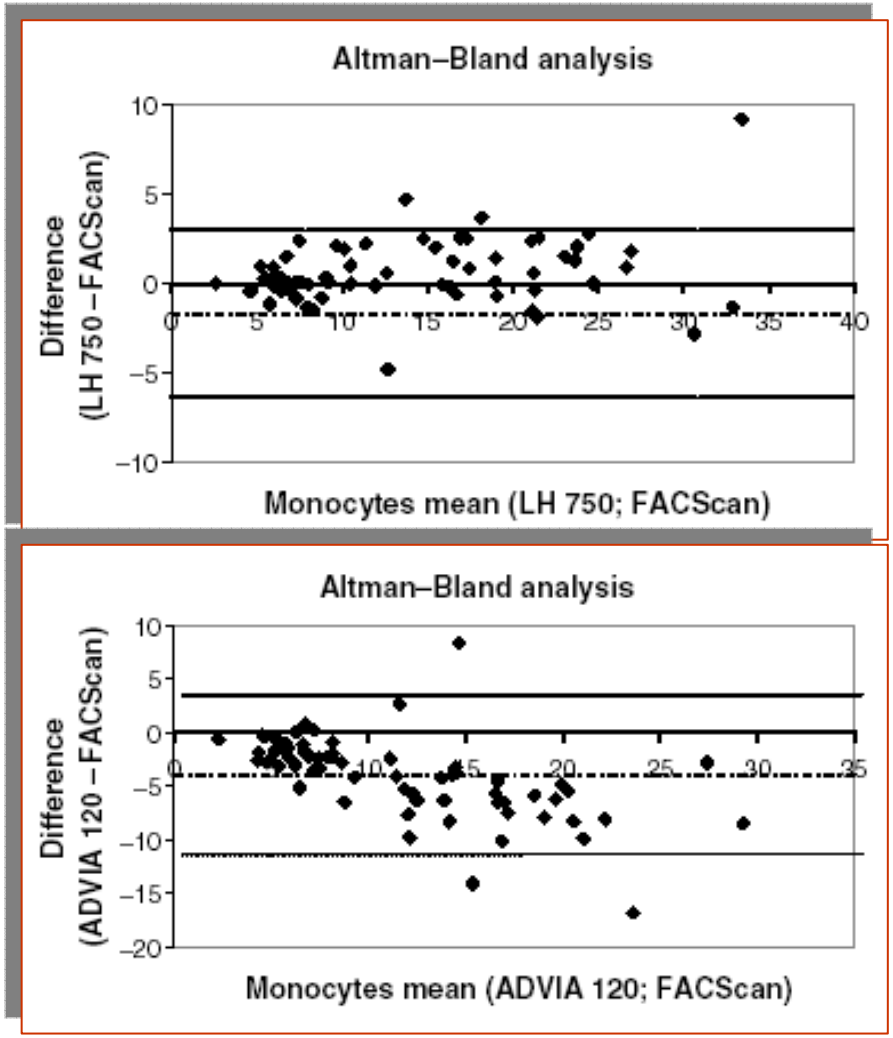


Table 3. Comparison of LH 750 and ADVIA 120 with FACScan: deming regression analysis data of 70 samples analysed side-by-side by the three instruments

	LH 750	ADVIA 120
Mean	14.21	9.51
SD	7.977	5.305
Reference mean*	13.58	13.58
P-value†	>0.05	<0.01
Mean‡	0.631	−4.06
95% CI	0.172–1.090	−3.13 to −4.99
SD	1.867	6.209
r-value	0.973	0.880
Intercept	0.139	1.047
Slope	1.036	0.623
S_{yx}	1.862	2.534

SD, standard deviation of difference.
*FACScan values.
†ANOVA with Tukey post-test.
‡Mean of difference.

E Grimaldi et al 2005

Sensibilità clinica

n. 496	100-Cell %	STKS %	NE8000 %	H2 %
Distributional false-abnormal	8.8	15.1	7.4	7.6
Distributional false-normal	29.9	6.1	8.9	13.5
Morphologic false-abnormal	0	17.1	6.2	3.1
Morphologic false-normal	18.6	4.2	12.2	21.3

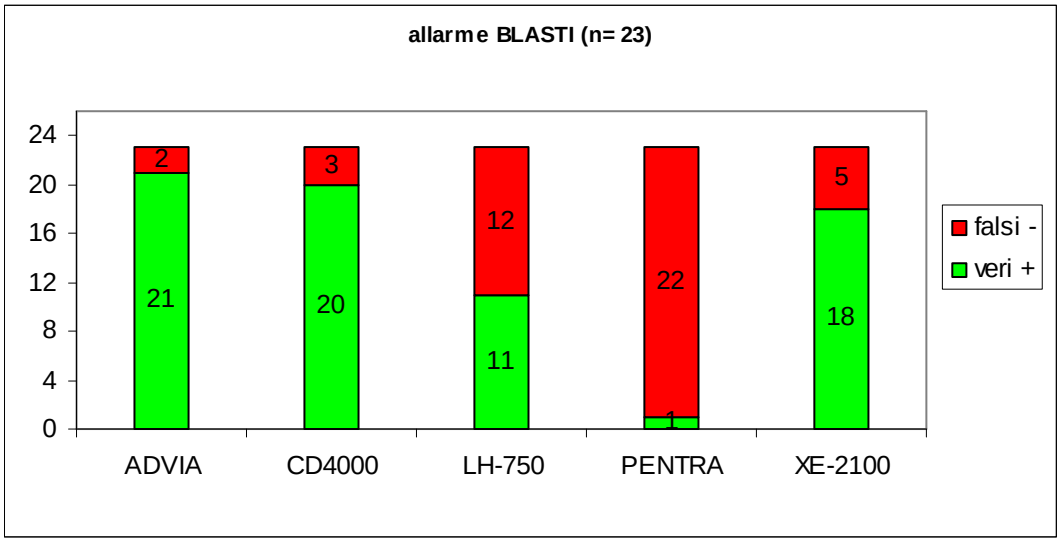
JA Koepke et al 1985

Tab. 9. Predictive values and efficiency of morphology flagging (samples = 113).

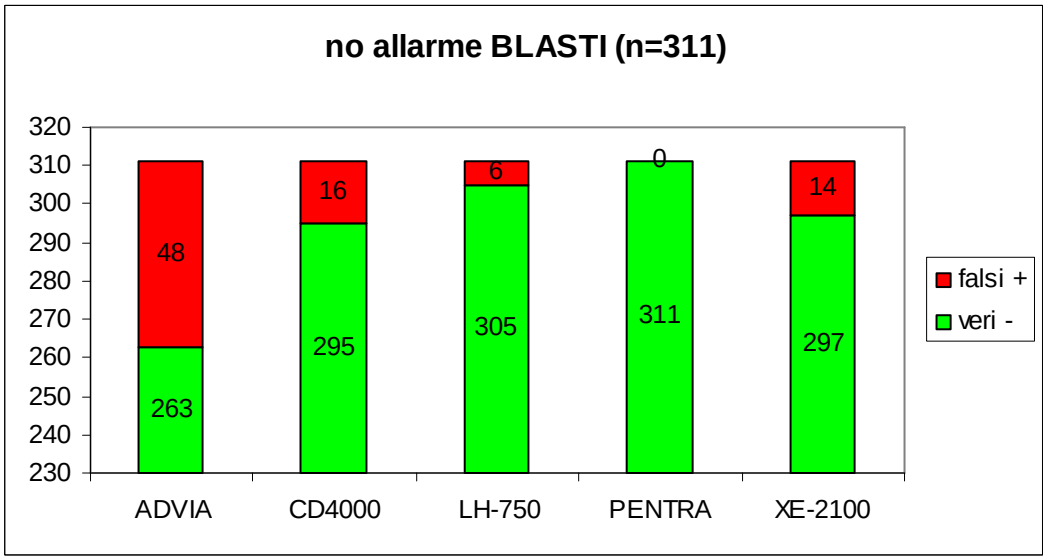
	Technicon H1				Sysmex NE 8000				Coulter STKS				Sequoia CD 3000	
	Immature granulocytes bands	Blasts	Atypical lymphocytes	Erythroblasts	Immature granulocytes bands	Blasts	Atypical lymphocytes	Erythroblasts	Immature granulocytes bands	Blasts	Atypical lymphocytes	Erythroblasts	Immature granulocytes bands	Erythroblasts
Sensitivity %	50.0	66.6	59.0	28.5	43.0	60.0	13.6	7.0	71.0	53.3	36.3	42.8	57.0	14.2
Specificity %	93.0	92.0	93.4	88.8	92.4	96.9	94.5	97.0	89.4	93.3	92.0	97.0	89.0	100.0
Predictive value % of a positive test	70.0	55.0	68.0	27.0	63.2	75.0	37.0	25.0	69.0	53.0	50.0	67.0	61.0	100.0
Predictive value % of a negative test	85.0	94.7	90.4	89.8	84.2	94.0	81.9	88.0	90.5	93.0	87.0	92.0	88.0	89.0
Efficiency %	82.3	88.5	86.7	81.4	80.8	91.1	78.8	85.8	85.0	88.3	81.8	90.5	82.0	89.3

M Buttarello et al 1993

Sensibilità blasti



GdS-E SIMeL 2003



Sensibilità clinica vs H-20 A allarmi (numerici + flag) globali

	Abbott CD4000	Abx Pentra 120	Bayer Advia 120	Coulter LH750	Sysmex XE2100
VP	11	9	13	10	10
VN	151	173	133	144	164
FP	28	6	45	35	16
FN	1	3	0	2	1
Sensibilità	91.6	75.0	100	83.3	90.9
Specificità	84.3	96.6	74.7	80.4	91.1
VPP	28.2	60.0	22.4	22.2	38.4
VPN	**99.3**	**98.3**	**100**	**98.6**	**99.4**

GdS-E SIMeL 2003

The main issue: Review Criteria

n. 13.298	Number	%
True positive	1483	11.20
False positive	2476	18.60
True negative	8953	67.30
False negative	386	2.90
Total number of samples	13298	

3% (2-4)
JR Krause
1990

False Negative Occurrences	%
Metamyelocyte, myelocyte, promyelocyte	52
Blast	1.3
Atypical lymphocyte	3.1
NRBC	6.6
RBC morphology	18.5
Platelet morphology	14.5
WBC morphology	4.0

PW Barnes et al 2005

Extended Differential Count

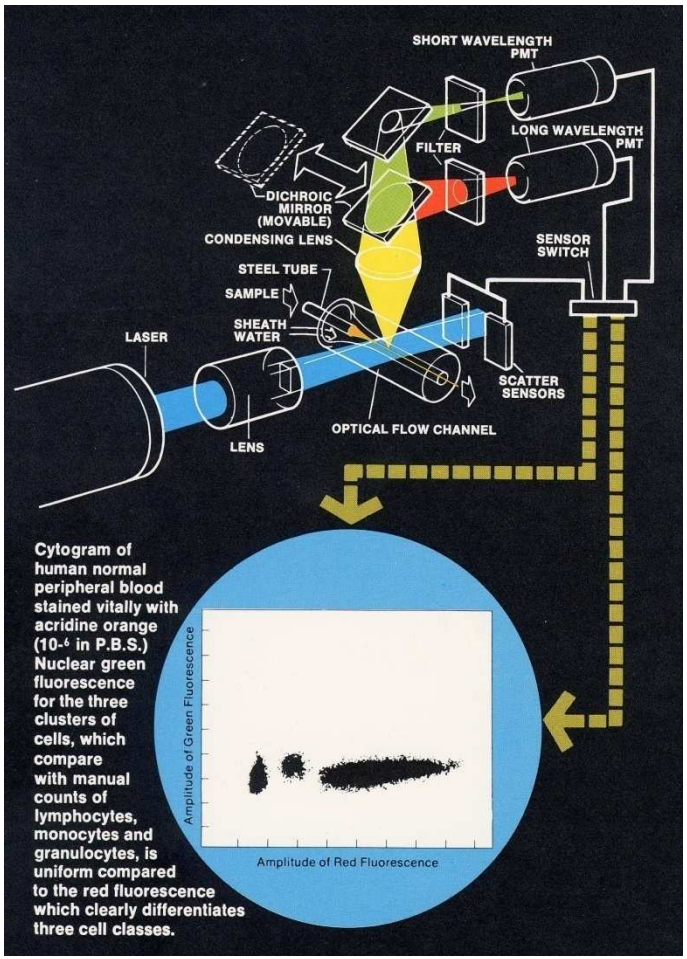
Traditional	Ref. Int.	Extended	Limit	Freq
Neutrophils	38-68	Left shift	Var	NA
Lymphocytes	22-50	IG	>1%	11%
Monocytes	5-11.4	NRBC	>1%	2%
Eosinophils	0.8-5.3	Blasts	>1%	0.7%
Basophils	0.2-1.0	Atypical L	>10%	0.3%
		HPC		NA
		Other		0.2%

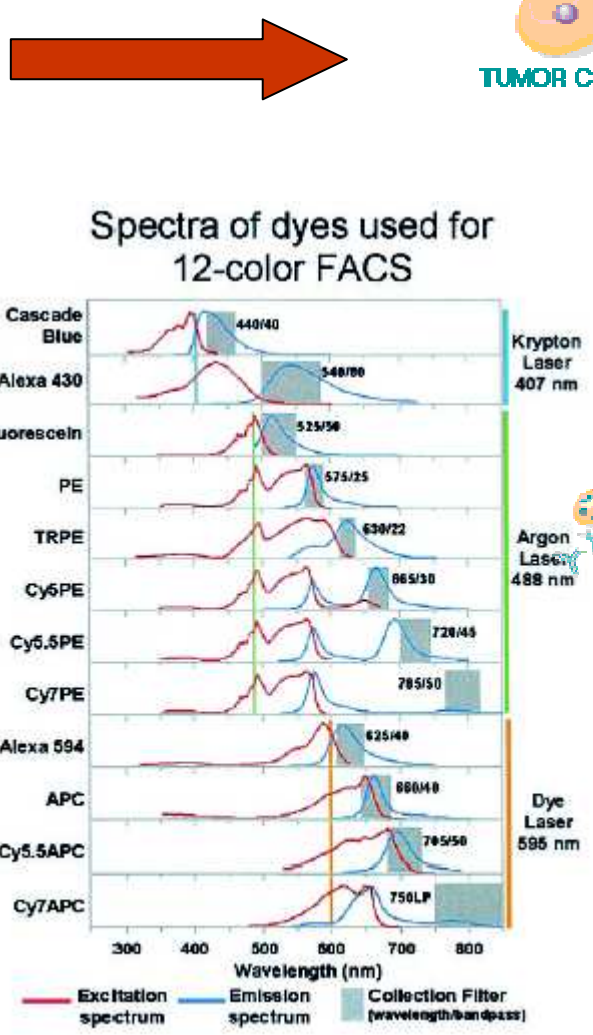
B Houwen 2001

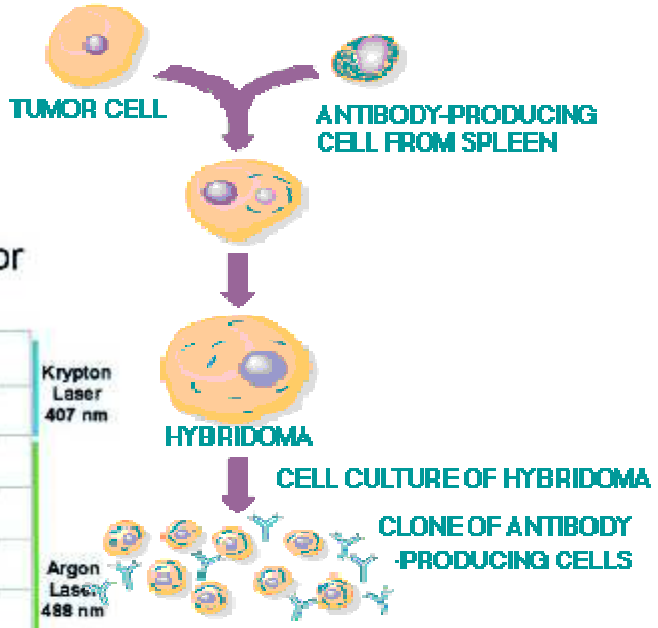
EDC: replacement of morphological analysis?

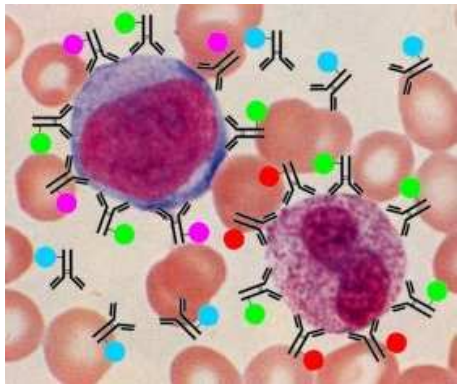
- At this moment left shift is not [expected to be part of the EDC], due to lack of agreement on the morphology of left-shifted cells. *B Houwen 2001*
- A pandemic problem … is an inability to distinguish between small lymphoid blasts, circulating small lymphoma cells, and normal lymphocytes. *PCJ Ward 2000*

Hematology without microscopy

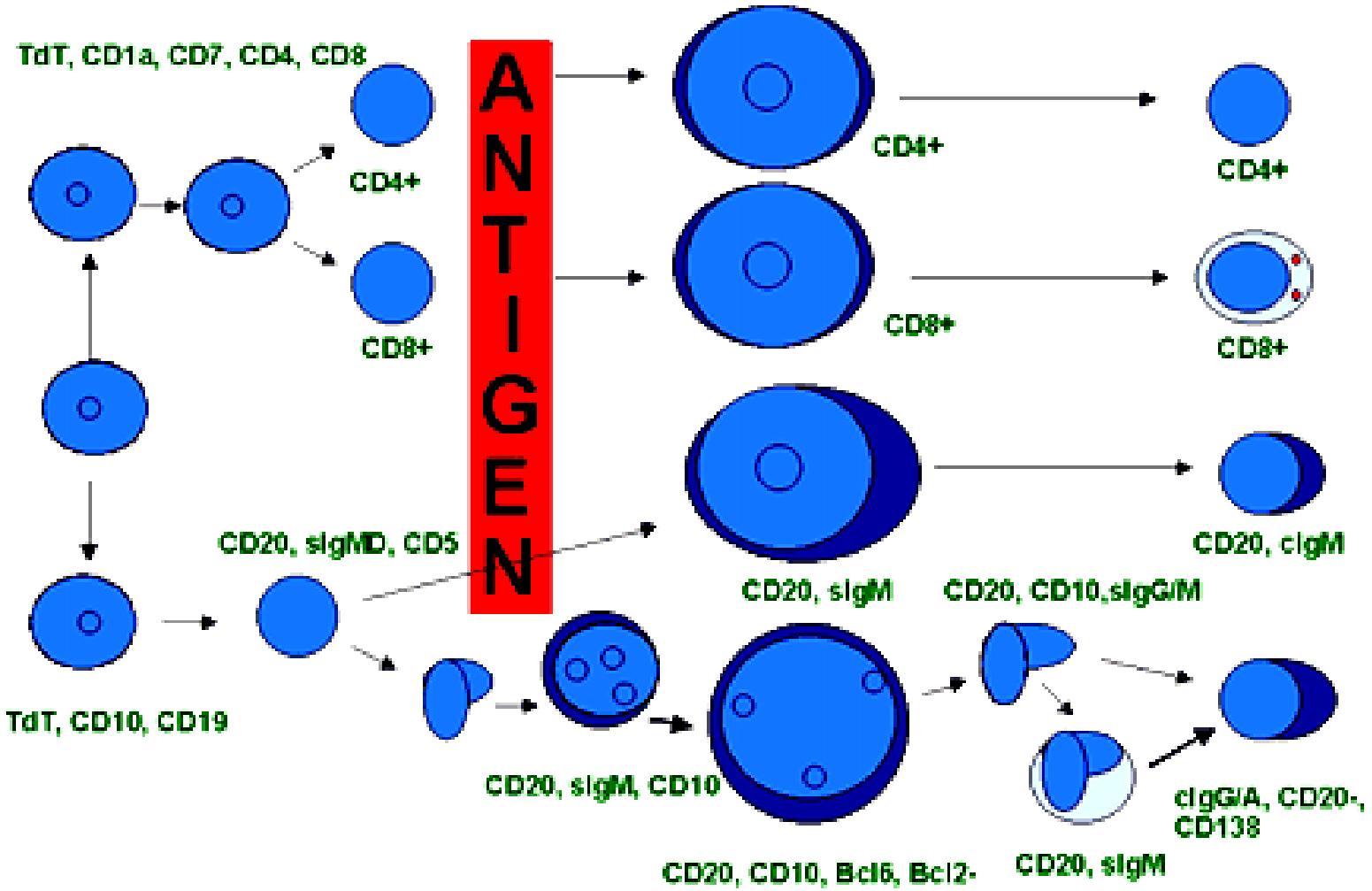




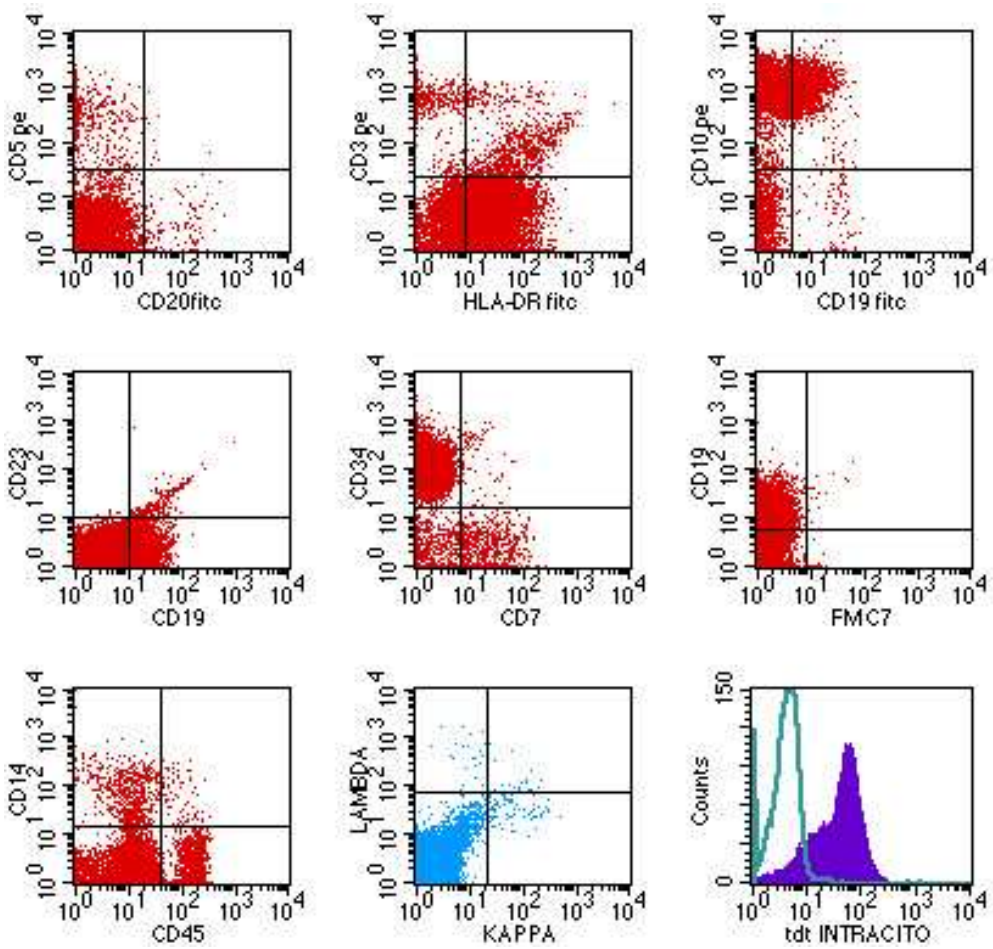




Changes in surface antigen expression characterize stages of T and B-cell differentiation

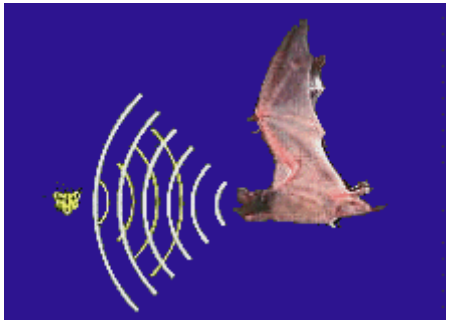


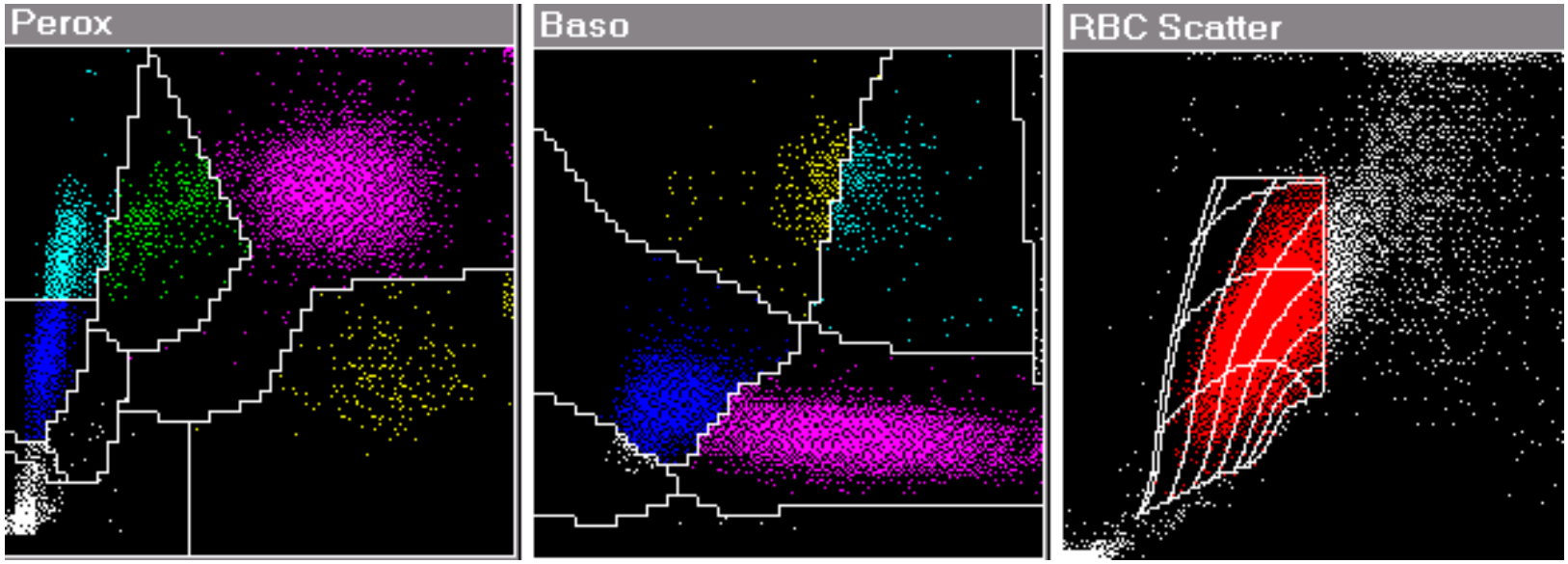
Phenotipic analysis of ALL



Citofluorimetria

- Il sistema concettuale interpretativo della citofluorimetria è “altro” da quello della morfologia ottica e del suo “doppio” citometrico
- “What is it like a bat?”





Emocromo di routine			
WBC:		11,13	x10³/µL
RBC:		4,83	x10⁶/µL
HGB:		12,3	g/dL
HCT:		38,7	%
MCV:	L	80,2	fL
MCH:	L	25,4	pg
MCHC:	L	31,7	g/dL
CHCM:	L	32,2	g/dL
CH:		25,7	pg
RDW:	H	15,5	%
HDW:		3,13	g/dL
PLT:		309	x10³/µL
MPV:		8,5	fL

Formula WBC di routine		%			x10³/µL	
WBC:					11,13	
Neutro:		60,5			6,73	
Linfo:		23,6	*		2,63	*
Mono:		3,5			0,39	
Eosino:		2,4			0,26	
Baso:	H	2,4	*	H	0,27	*
LUC:	H	10,0	*	H	1,11	*
LI:					2,31	
MPXI:					-0,9	
WBCP:					10,71	

Mantellare

Fenotipo

CD5+bright

CD23-

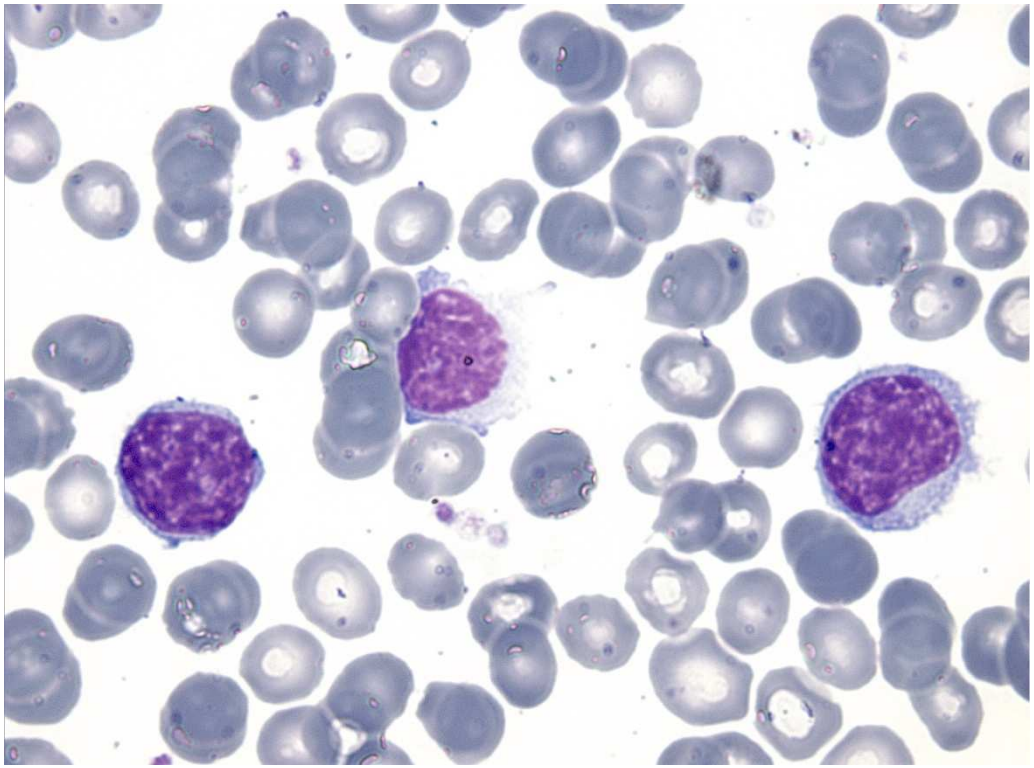
CD20+

CD10-

FMC7+/-

sIg+bright

CD54+

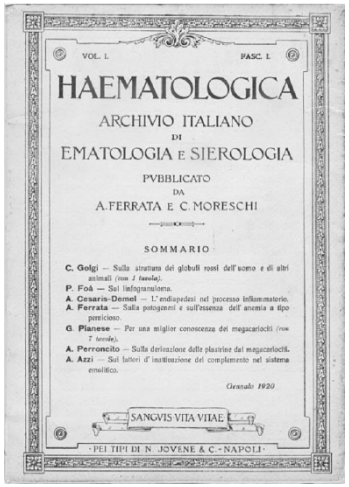


La nascita della Medicina moderna

- ***Rudolf Ludwig Karl Virchow***
- *Die Cellularpathologie* (1858)
- “con l’avvento della dottrina di Virchow, la clinica cede il posto alla patologia e il laboratorio diviene il simbolo della clinica”
- “la nascita dell’ematologia dalla citologia è parte del processo di “specializzazione” della medicina, tipico della seconda metà del XX secolo”

Ematologia di Laboratorio: una disciplina clinica

- Morfologia del sangue normale e patologico (1912)
- Le Emopatie (1919-21)


VOL. I. FASC. I.

HAEMATOLOGICA

ARCHIVIO ITALIANO DI EMATOLOGIA E SIEROLOGIA

PVBBLICATO DA A. FERRATA E C. MORESCHI

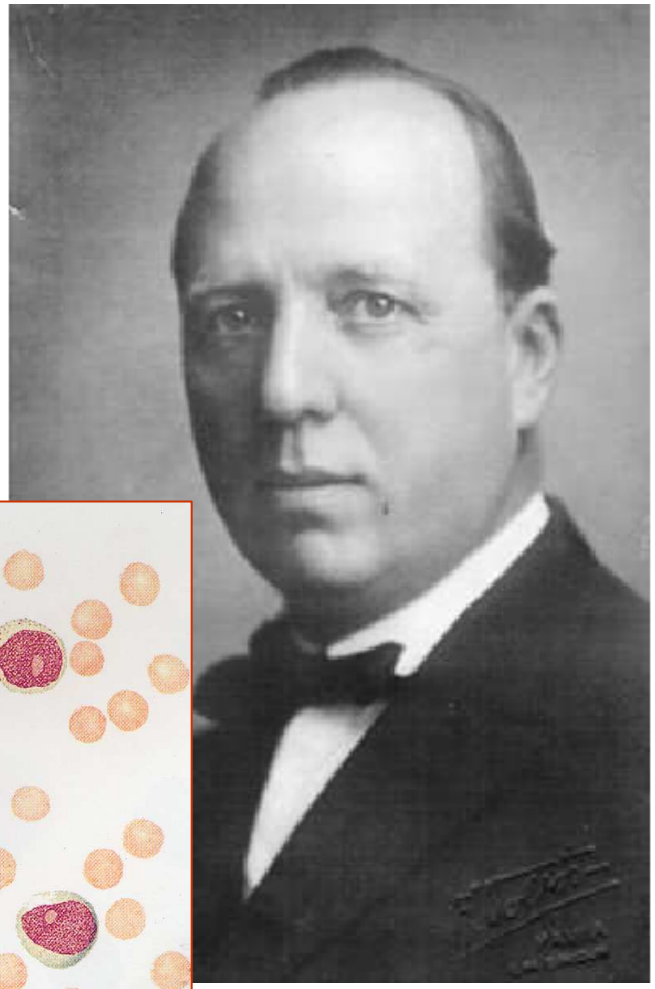
SOMMARIO

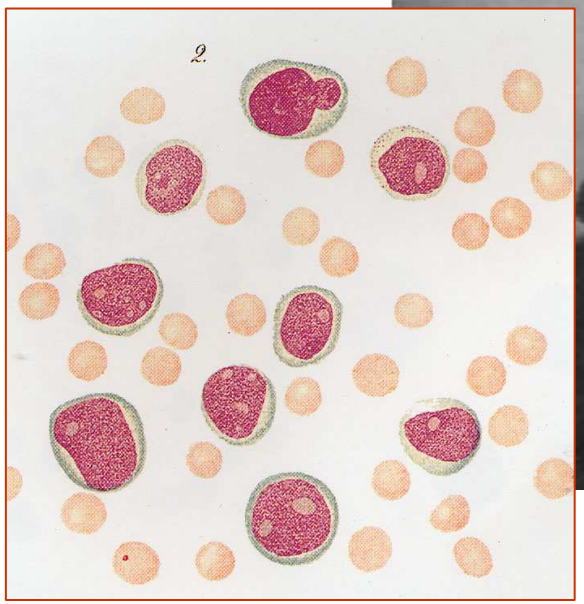
C. Golgi — Sulla struttura dei globuli rossi dell'uomo e di altri animali (con 3 tavole).
P. Foà — Sul linfogranuloma.
A. Cesaris-Demel — L'endiapedesi nel processo infiammatorio.
A. Ferrata — Sulla patogenesi e sull'essenza dell'anemia a tipo perniciosa.
G. Pianese — Per una miglior conoscenza dei megacariocti (con 7 tavole).
A. Perroncito — Sulla derivazione delle piastrine dai megacariocti.
A. Azzi — Sul fattori d'inattivazione del complemento nel sistema emolitico.

Granado 1920

SANGVIS VITA VITAE

PEI TIPI DI N. JOVENE & C. - NAPOLI



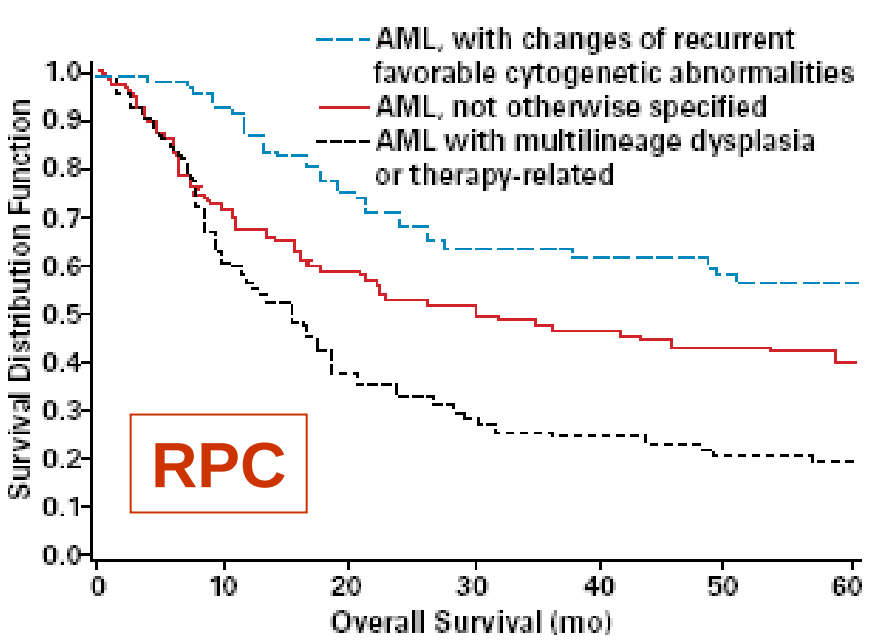


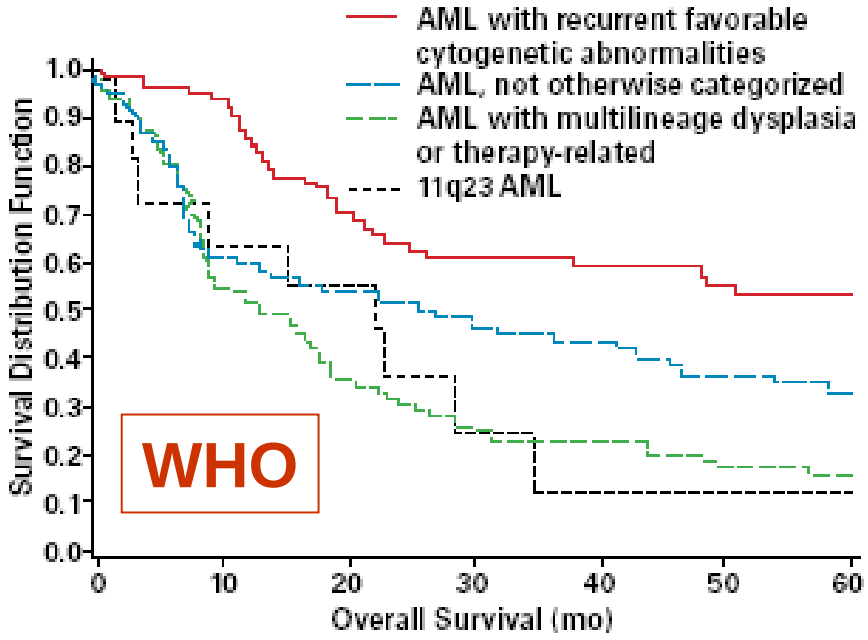
Sixty years of Haematology

- In the late 1940s haematology was still largely a laboratory discipline.
- During the past 60 years, the haematologist has become a different sort of person. In many countries he, or increasingly she, has moved out of the laboratory and become a clinician, often to the detriment of laboratory haematology. Subspecialisation continues apace. No longer is it possible to have grasp of either laboratory or clinical haematology in their entirety, let alone both.
- Haematology saw the first demonstration of a specific recurrent cytogenetic abnormality in association with a specific neoplasm, and this was followed by the demonstration of specific molecular genetic abnormalities associated with specific subtypes of leukaemia and lymphoma … accompanied and followed by major therapeutic advances explicable on a molecular basis…
- In the next 60 years? Laboratories will become even more automated and the role of computers will increase even further; perhaps artificial neural networks will replace some functions of the pathologist. Haematology will become increasingly molecular, both in its diagnostic and in its therapeutic approach.

BJ Bain 2005

Prognostic Impact of AML Classification

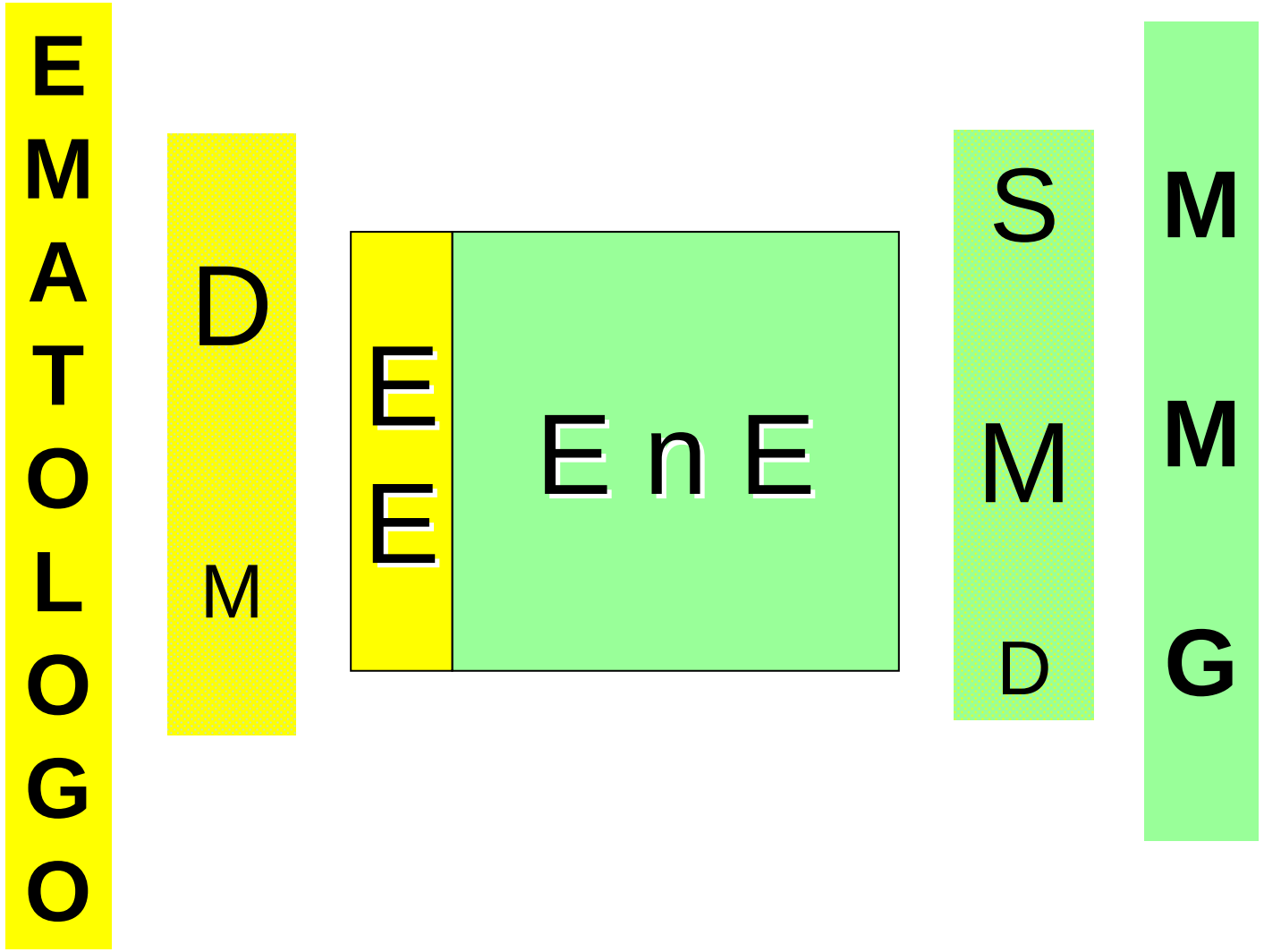




The combined group - AML therapy related, AML arising from MDS, AML with dyspasia - (n = 114), however, had a lower 5-year overall survival (18.4%; 95% CI, 11.1%-25.7%) compared with cases of AML without associated myelodysplastic changes (n = 186; 5-year survival, 46.7%; 95% CI, 39.3%-54.1%; *P* < .0001).

DA Arber et al 2003

Ematologia di Laboratorio



Anemia

- Anemia occurs commonly:
- Anemia impact mortality
- Anemia impacts morbidity
- Anemia impacts QOL
- Anemia management needs improvement

AR Nissenson et al 2003

PREVALENCE
5.7-5.9% (infants-women)
7.5-12%♂ >65y & >75 y
15-25%♀>65y & >75 y

ACD
30-70% chronic liver diseases
27% rheumatoid arthritis
28-55% HIV
21% inflammatory bowel disease
30% CHF
30-60% cancer
(27% chemo/radiation therapy)

Anemia: diagnosis

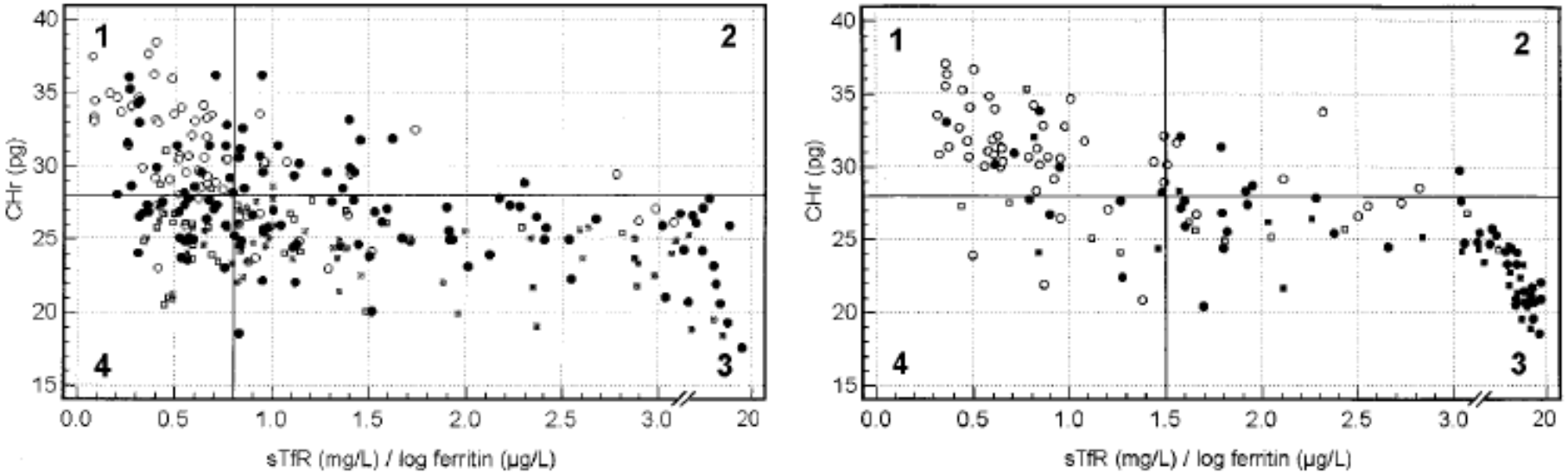


Fig. 5. Diagnostic plots for the identification of ID in anemic patients with (*left*) and without (*right*) APR.

	IDA (n = 72)				ACD[a] (n = 102)				CRA (n = 211)				Pregnancy (n = 47)			
	CRP <5 mg/L		CRP >5 mg/L		CRP <5 mg/L		CRP >5 mg/L		CRP <5 mg/L		CRP >5 mg/L		CRP <5 mg/L		CRP >5 mg/L	
Quadrant	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1					23	22.5	19	18.6	53	25.1	48	22.9	1	2.1	1	2.1
2					1	1.0	6	5.9	5	2.4	22	10.4	2	4.2	5	10.6
3	55	76.3	17	23.7			18	17.6	8	3.8	44	20.8	21	44.6	14	29.8
4					7	6.8	30	29.4	4	1.9	27	12.8	3	6.4		

[a] Excluding CRA patients.

C Thomas, L Thomas 2002

Ematologia di Laboratorio

1) fornire informazioni e consulenza,

2) per la diagnosi, screening e monitoraggio di malattie ematologiche (ematologia ematologica) o di anomalie ematologiche nel corso di malattie non primitivamente ematologiche (ematologia non ematologica)

3) attraverso una rete di mezzi tecnici e disciplinari (citometrici, morfologici, citofluorimetrici, biochimici, molecolari,…)

4) su materiali di pazienti umani.

La logica diagnostica dell'Ematologia di Laboratorio

- Metodologia di approccio al paziente ematologico, non all'esame emocromocitometrico
- Integrazione degli strumenti disponibili (morfologia, emocitometria, citochimica, citofluorimetria, citogenetica, biologia molecolare)
- Validazione "sample & patient oriented"
- Comunicazione efficace dei risultati

Logica diagnostica dell'Ematologia di Laboratorio. GdSE 1990

Le basi della conoscenza

ottima e aggiornata conoscenza

- *ematologia di laboratorio*
  - *Tecnologia utilizzata*
  - *Nuove tecnologie*
- *ematologia clinica*
  - *Diagnosi*
  - *Prognosi*
  - *Terapia*

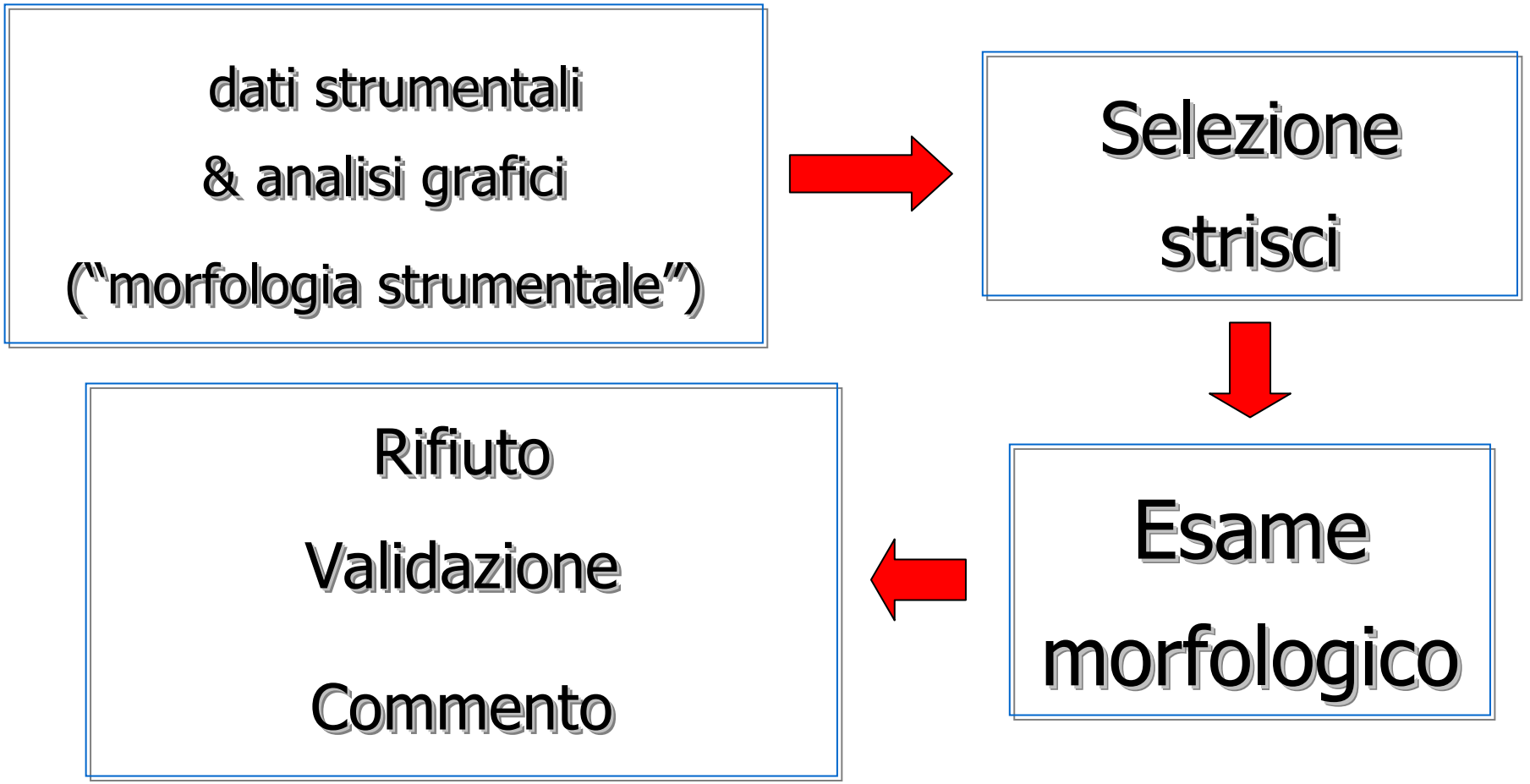
Revisione morfologica

- Notizie cliniche
- Allarmi strumentali
  - Efficienza
    - revisione 2-20% (*GdS E 2003*); 5-30% USA (*PCJ Ward 2000*); 5-40% UK (*M J Galloway, J C Osgerby 2006*); 29.8% (*ISLH 2005*)
  - Efficacia
    - *JR Krause 1990*: FP 8-15%; FN 2-4%
    - *ISLH 2005*: FP 18.60%; FN 2.86% (TP 11.2%)

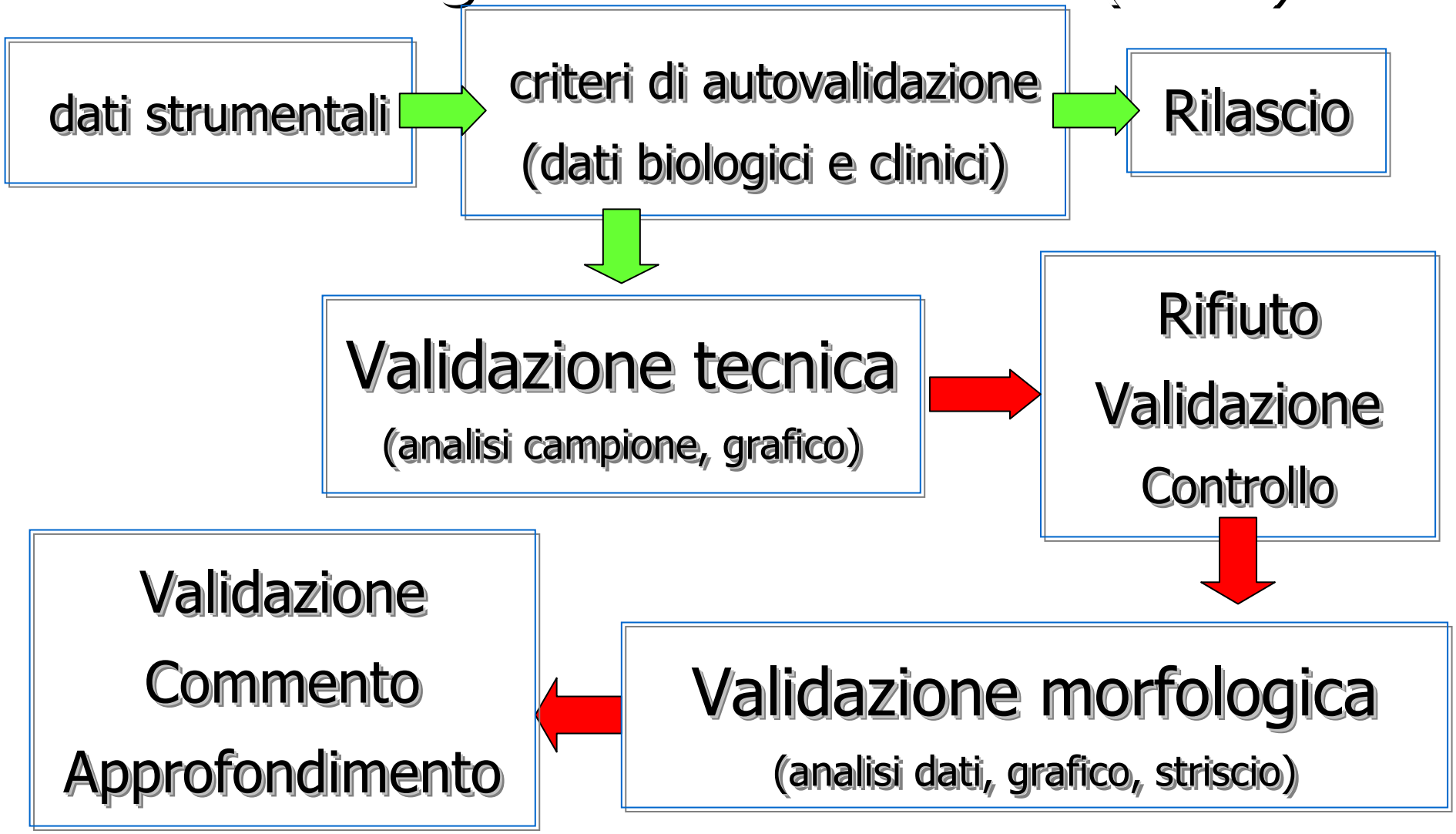
Evoluzione della tecnologia e ruolo del medico di laboratorio

- Validare sul campo i vantaggi teorici alla luce delle necessità cliniche
- Approfondire i suggerimenti strumentali, con la scoperta di nuove indicazioni
- Suggerire all'industria il superamento dei limiti e problemi riscontrati

Validazione ed interpretazione in Ematologia di Laboratorio (old)



Validazione ed interpretazione in Ematologia di Laboratorio (new)



Key word is communication

- Routine visits by the clinician to the laboratory…

R Hillman 2001

- Part of the laboratorian's role to educate clinicians about the usefulness of certain parameters…

B Howen 2005

La rete dei rapporti comunicativi
GdSE 1990

Mission

1. Promuovere lo studio e la conoscenza dell'ematologia di laboratorio
2. Formare medici di laboratorio esperti nella diagnostica ematologica
3. Standardizzare le metodiche, utilizzare pienamente i vantaggi della tecnologia
4. Perseguire l'appropriatezza attraverso linee-guida e referti interpretativi

Morfologia/Morfologie

“Si vorrebbe essere riusciti a documentare l’interesse che trasfigura il fenomeno morfologico quand’esso è messo in relazione col fenomeno funzionale, cosicché sempre si ribadisce il potere interpretativo e l’efficacia formativa che la morfologia possiede, nella ricerca e rispettivamente nell’educazione *ematologica*.”

A Ascenzi, G Mottura 1970

Domine, ut videam

Luca 18,41