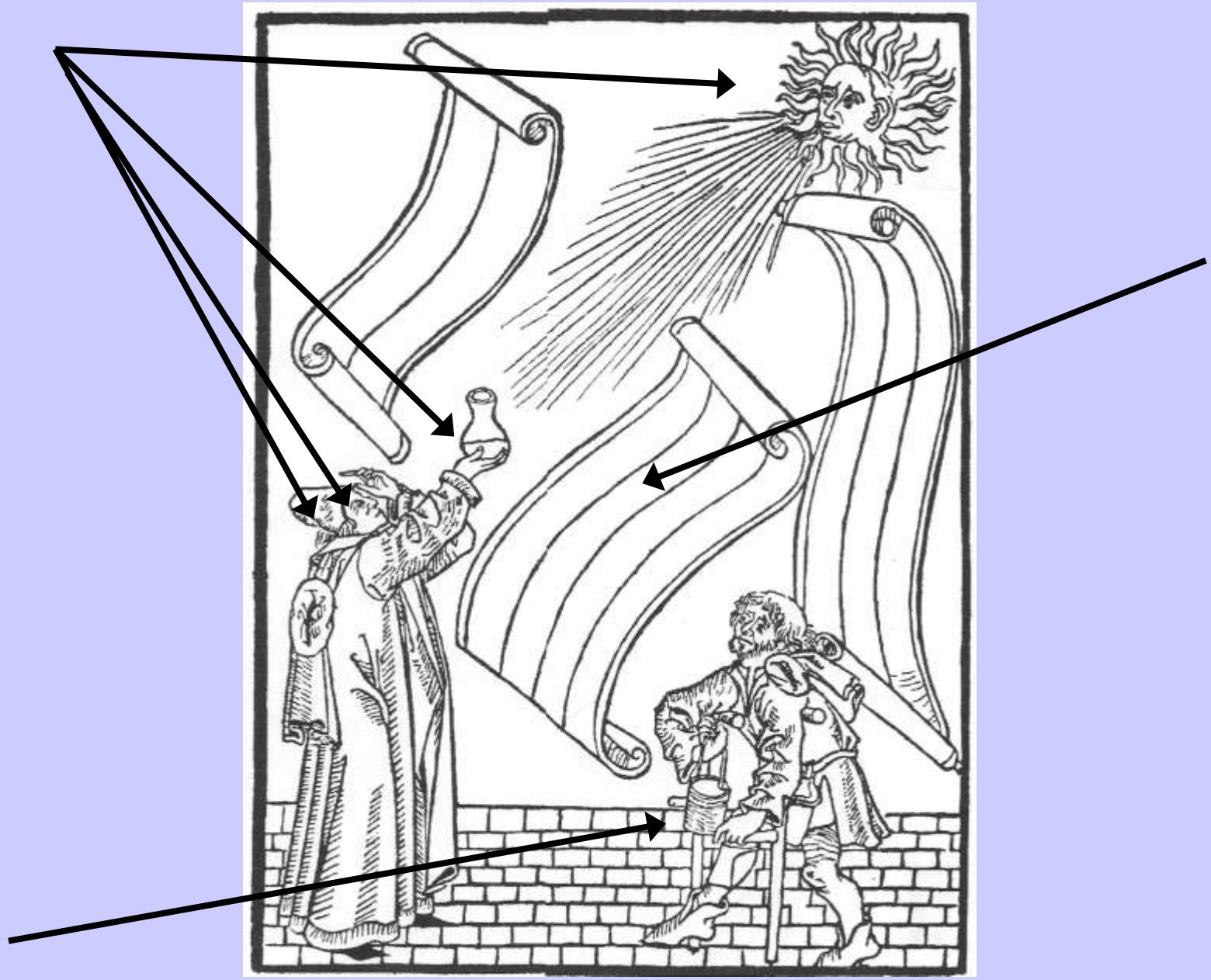
Diagnostic pathways for exclusion and diagnosis of kidney Diseases. The role of urine sediment and urine protein differentiation

Walter G. Guder

Munich

Rijeka, September 24. 2015



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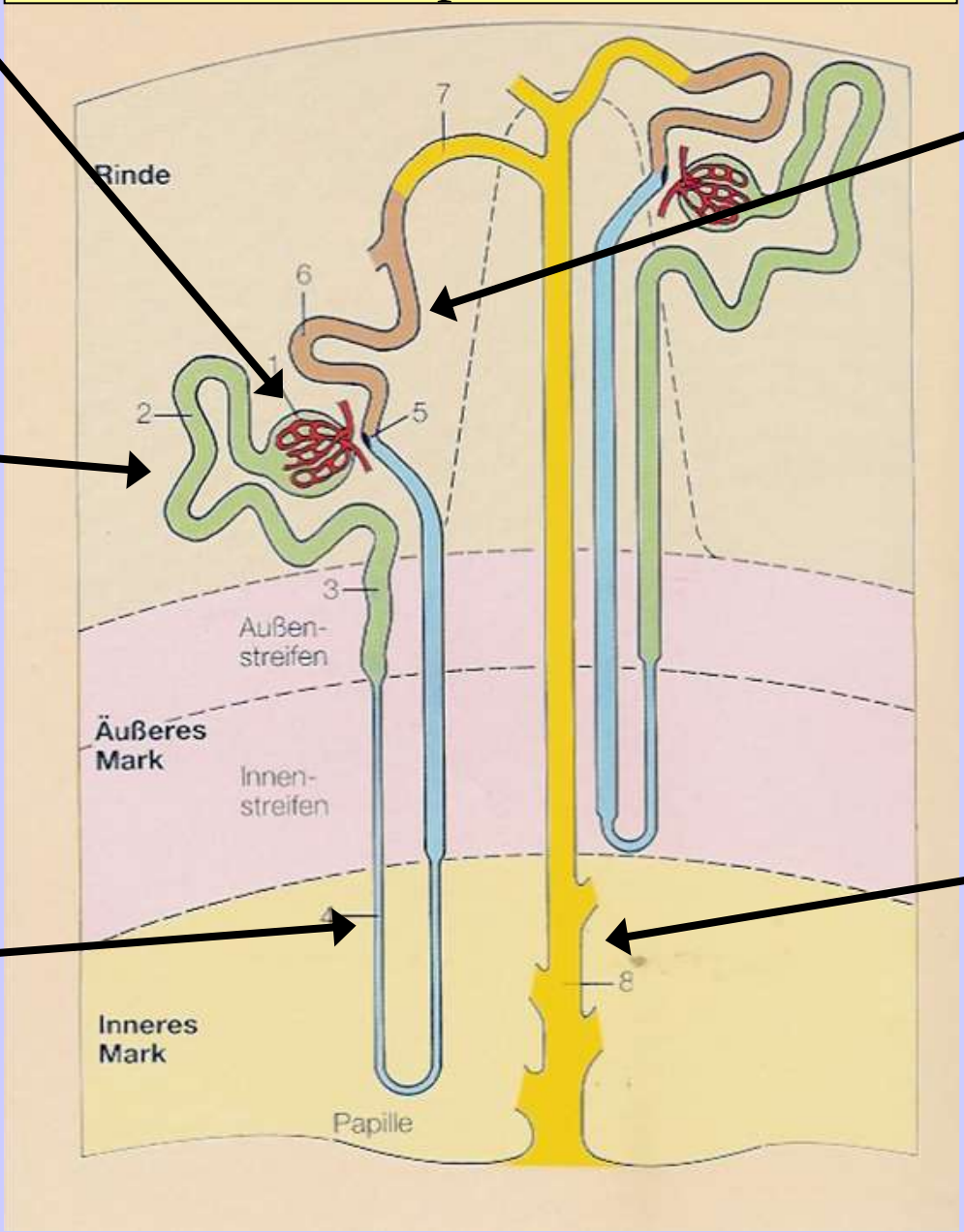
Nephron



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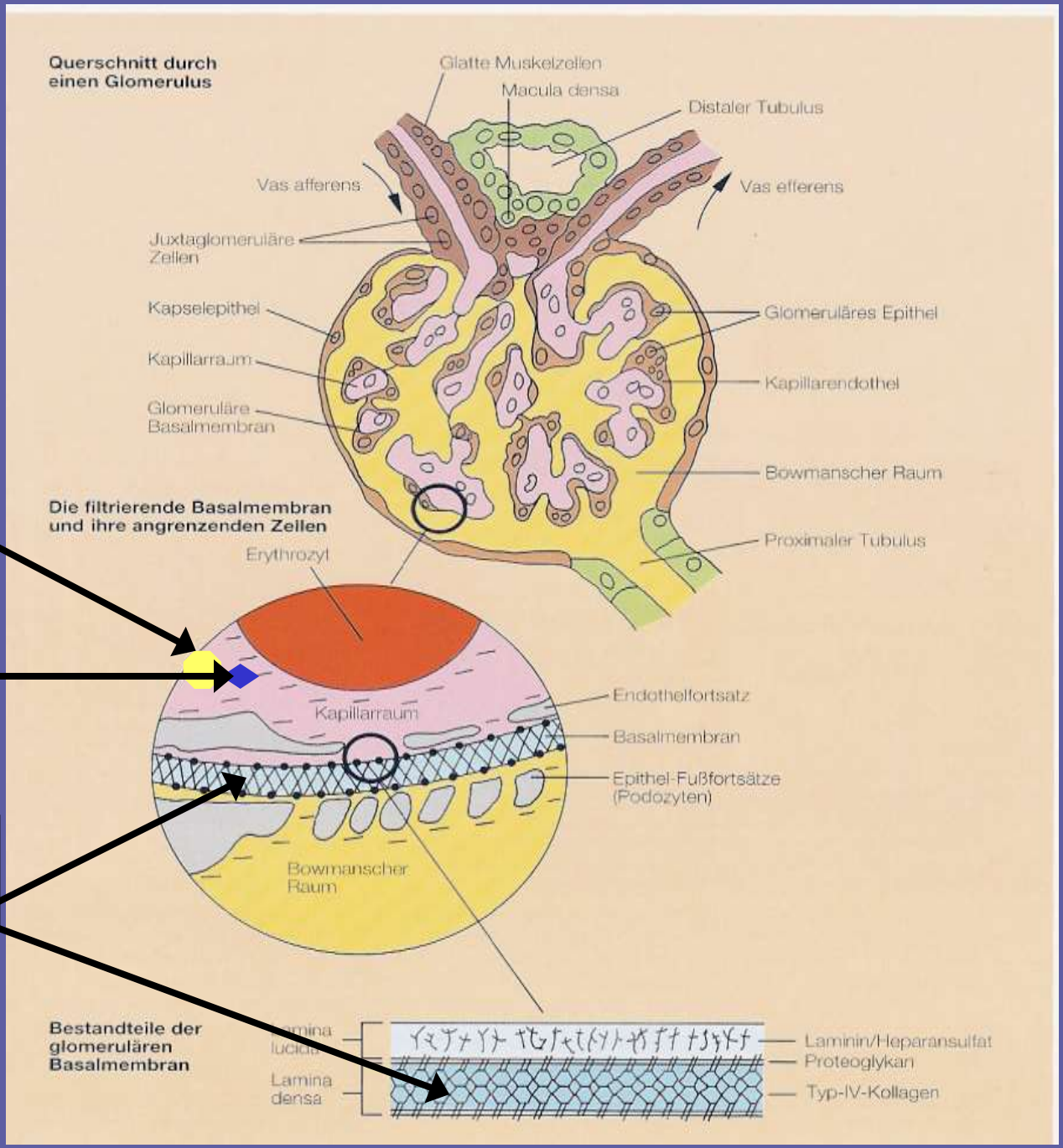
Glomerulus

albumin

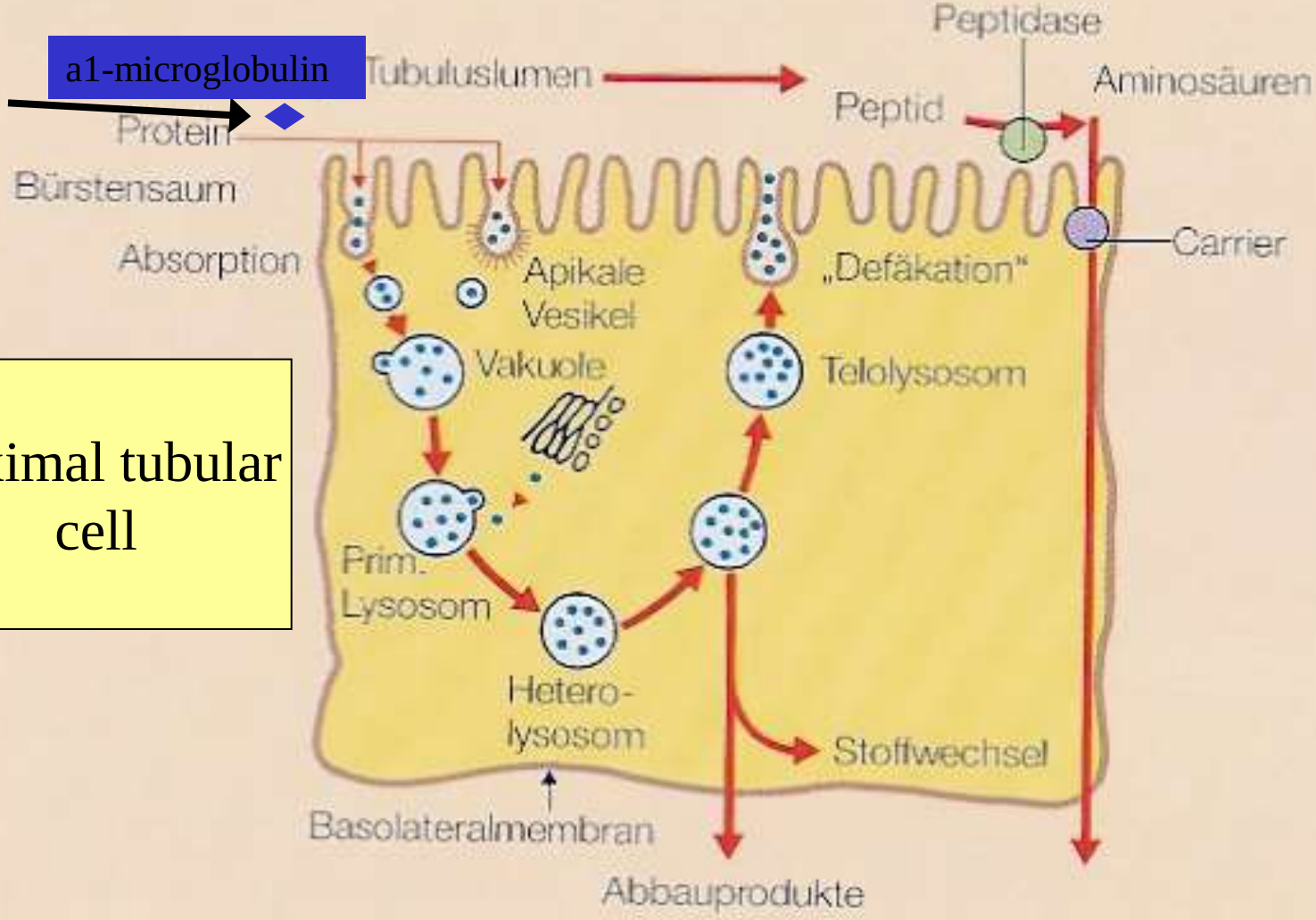
IgG

a1-mikroglobulin

Basement membrane

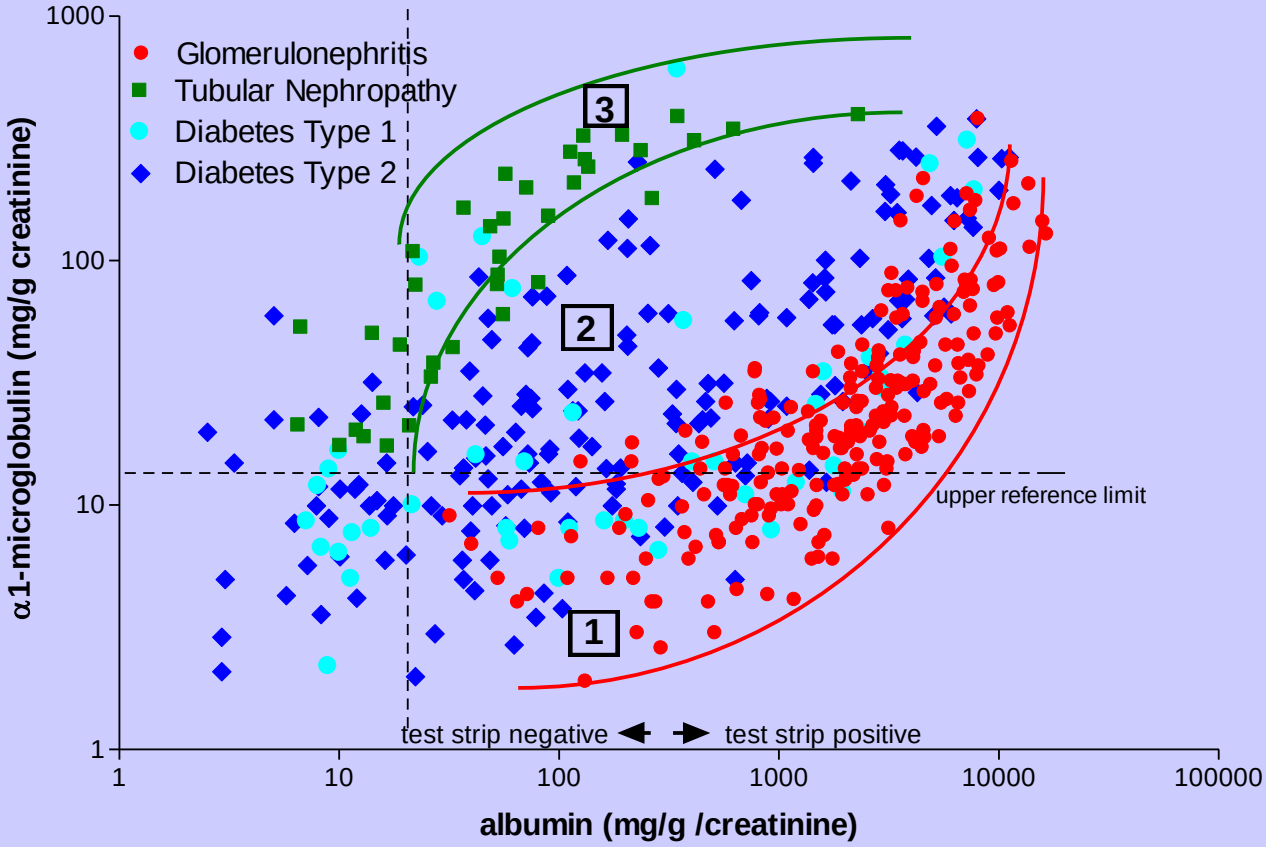


Tubular mechanism of protein reabsorption



Proximal tubular cell

Glomerular and tubular proteinuria in patients with diabetic nephropathy, compared to glomerular and tubulo-interstitial nephropathies



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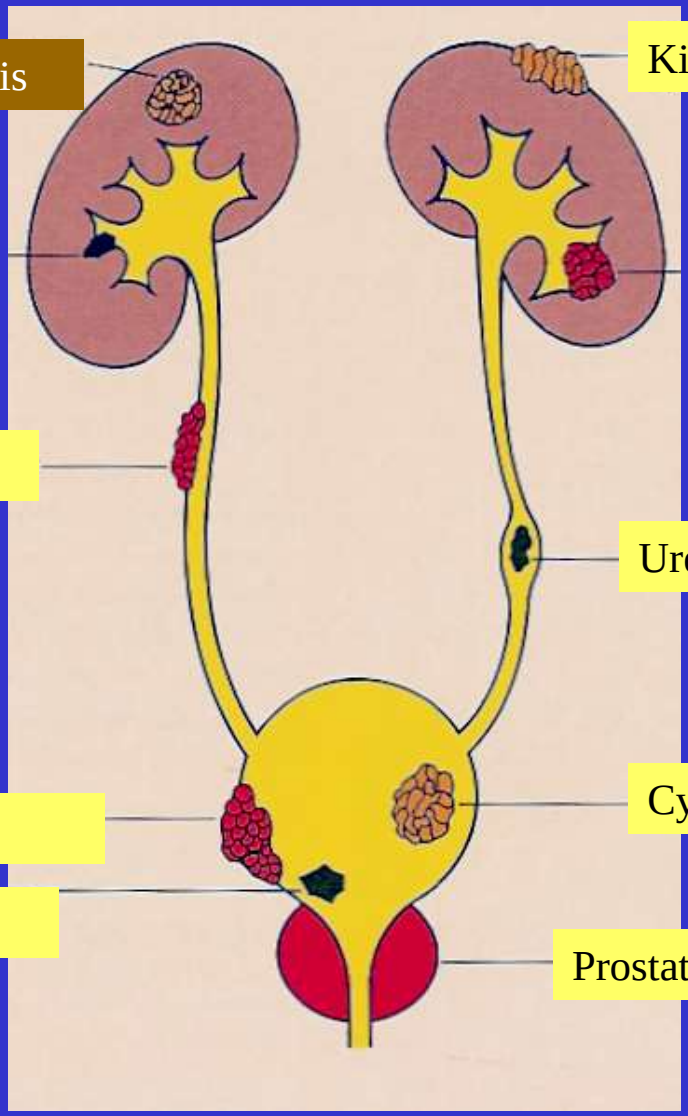
Differentiation of hematuria

Possible causes of hematuria



Glomerulonephritis

Kidney tuberkulosis

Kidney stone

Hypernephroma

Ureter tumour

Ureter stone

Bladder cancer

Cystitis

Bladder stone

Prostata adenoma

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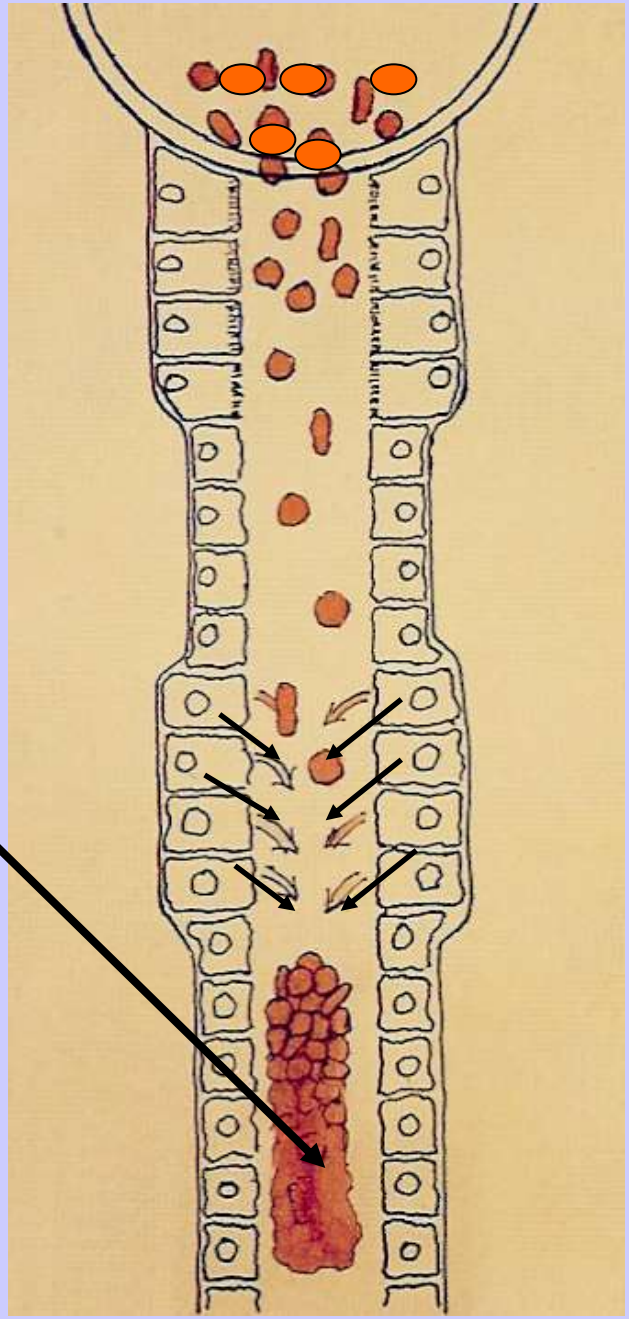
Erythrozytenzylinder



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Erythrozytenzylinder (Sediment)

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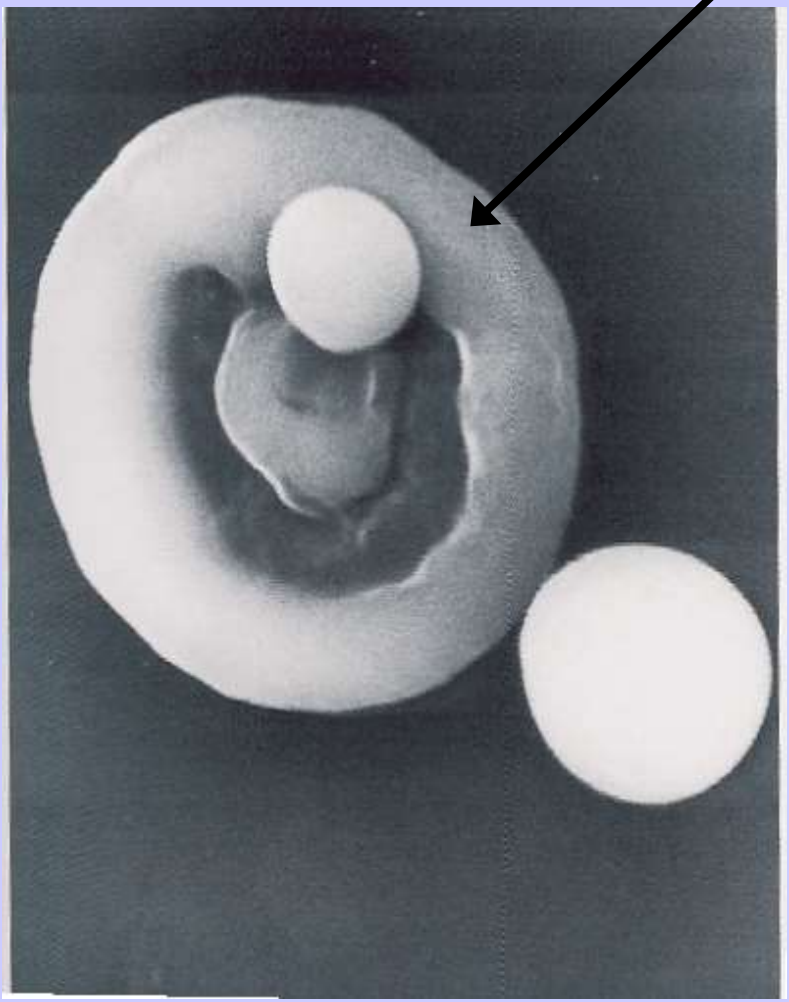
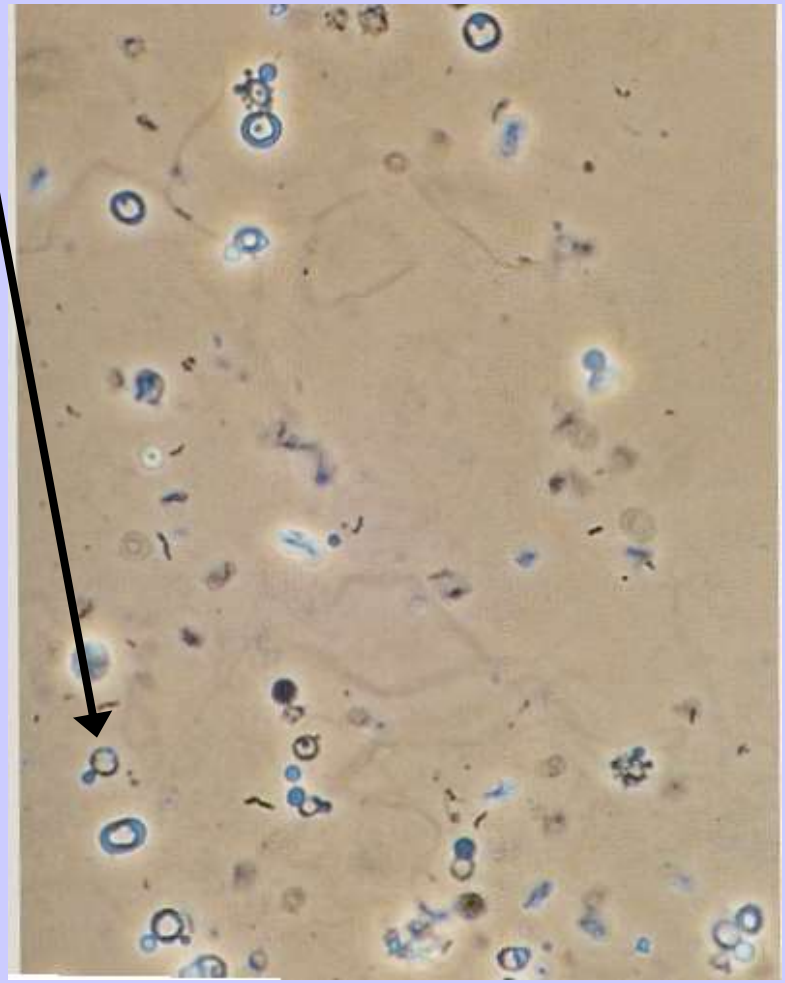
Akanthozyten





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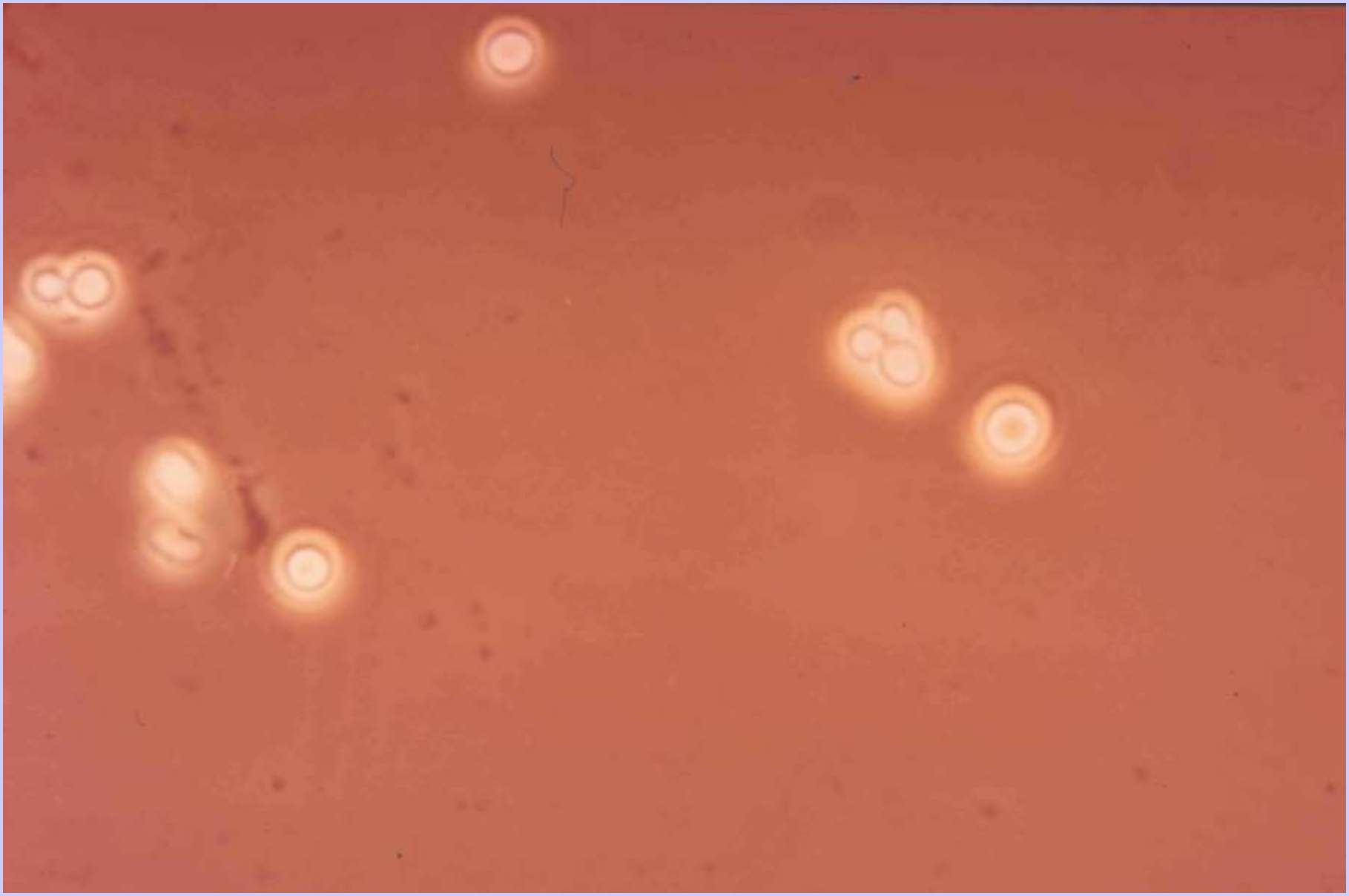

Hefezellen

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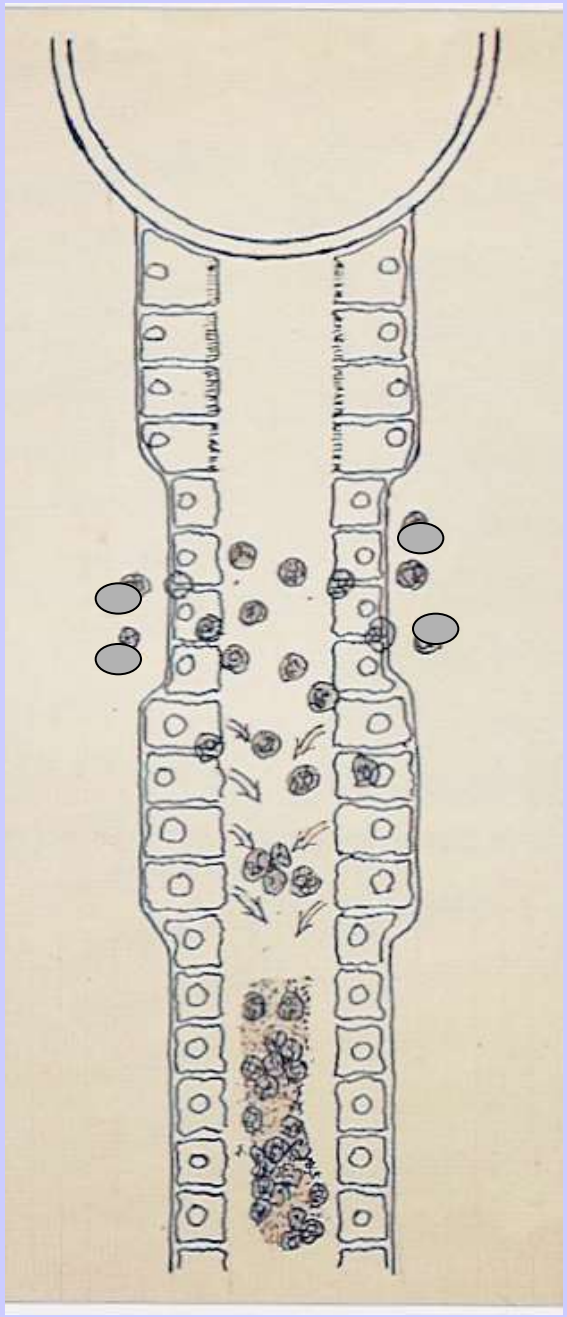
Leucocyturie

?

Leukozyten-Zylinder



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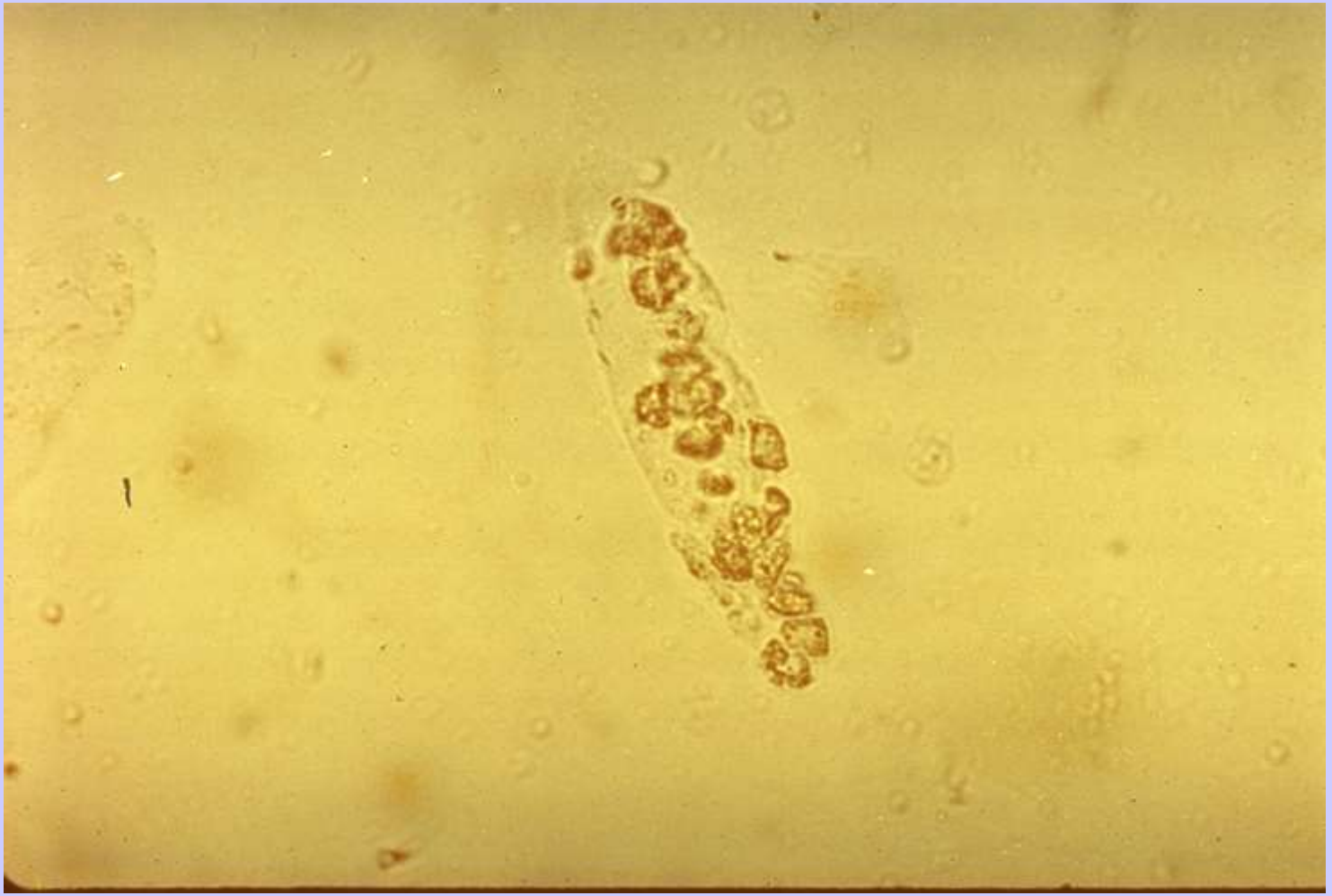
Leukozytenzylinder



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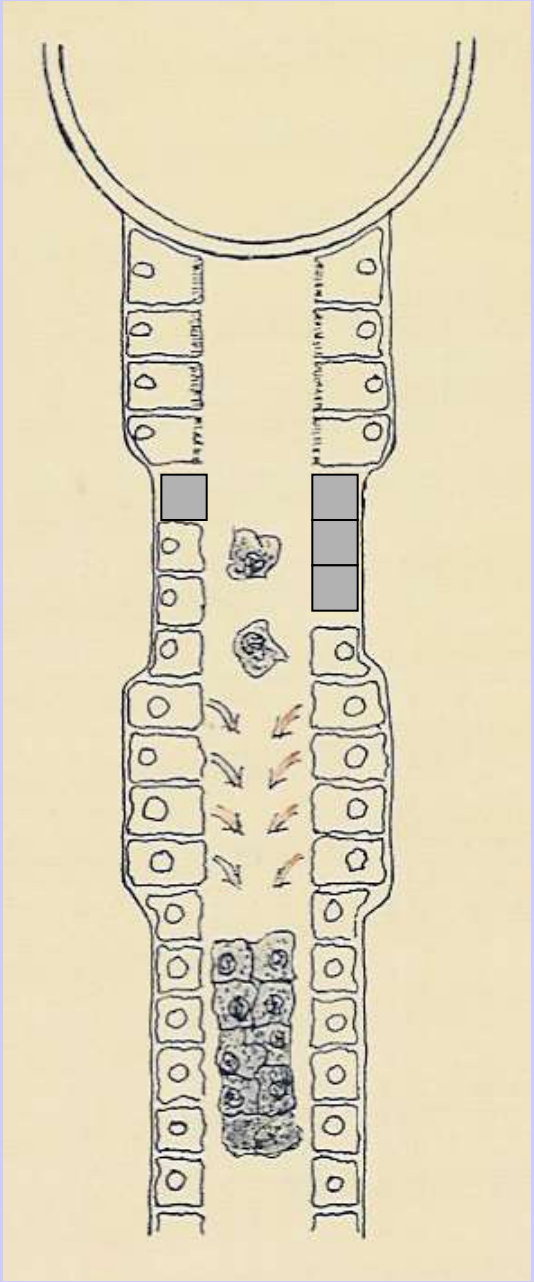
Epithel-Zylinder



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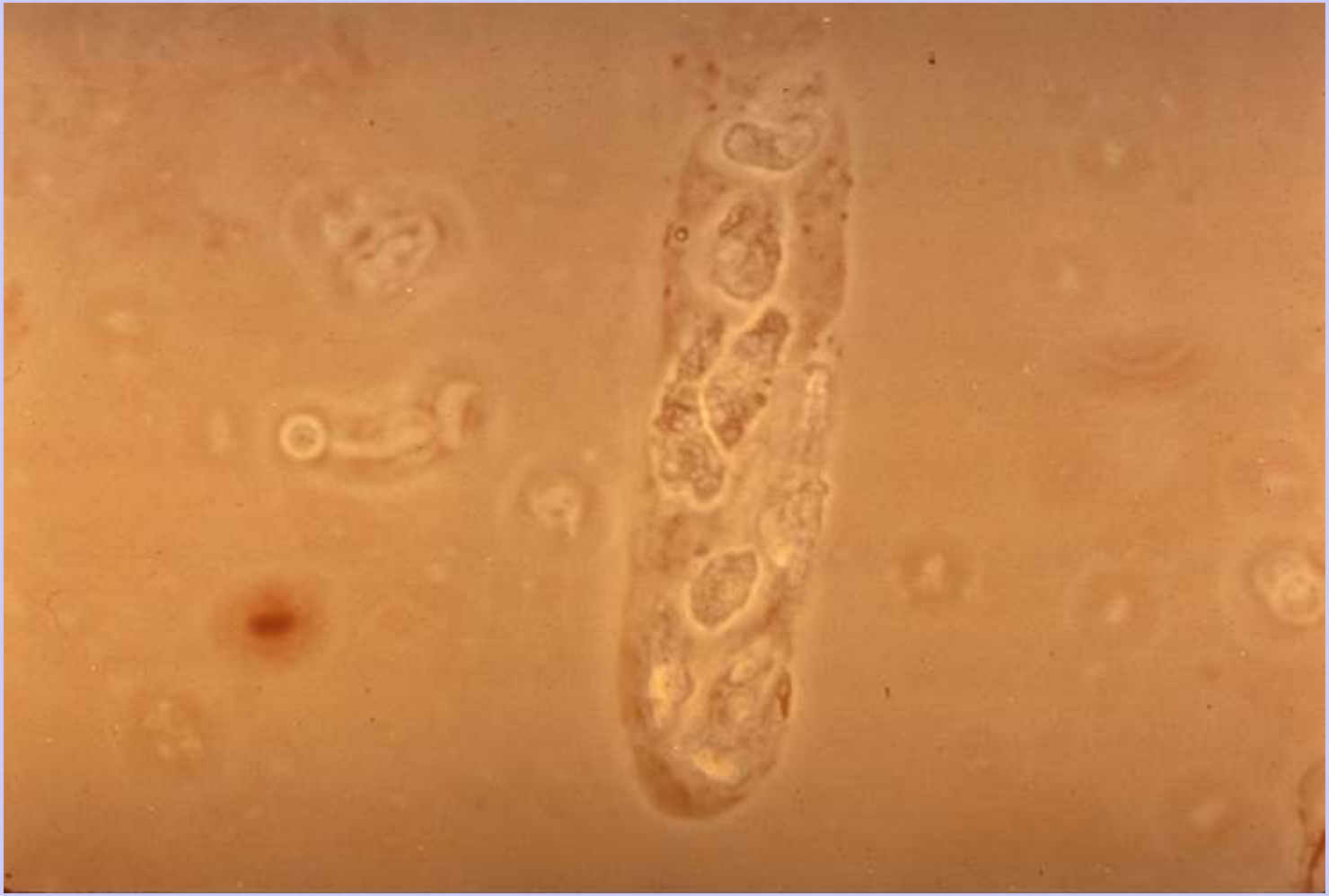
Epithel-Zylinder



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Erythrozytenzylinder (Sediment)

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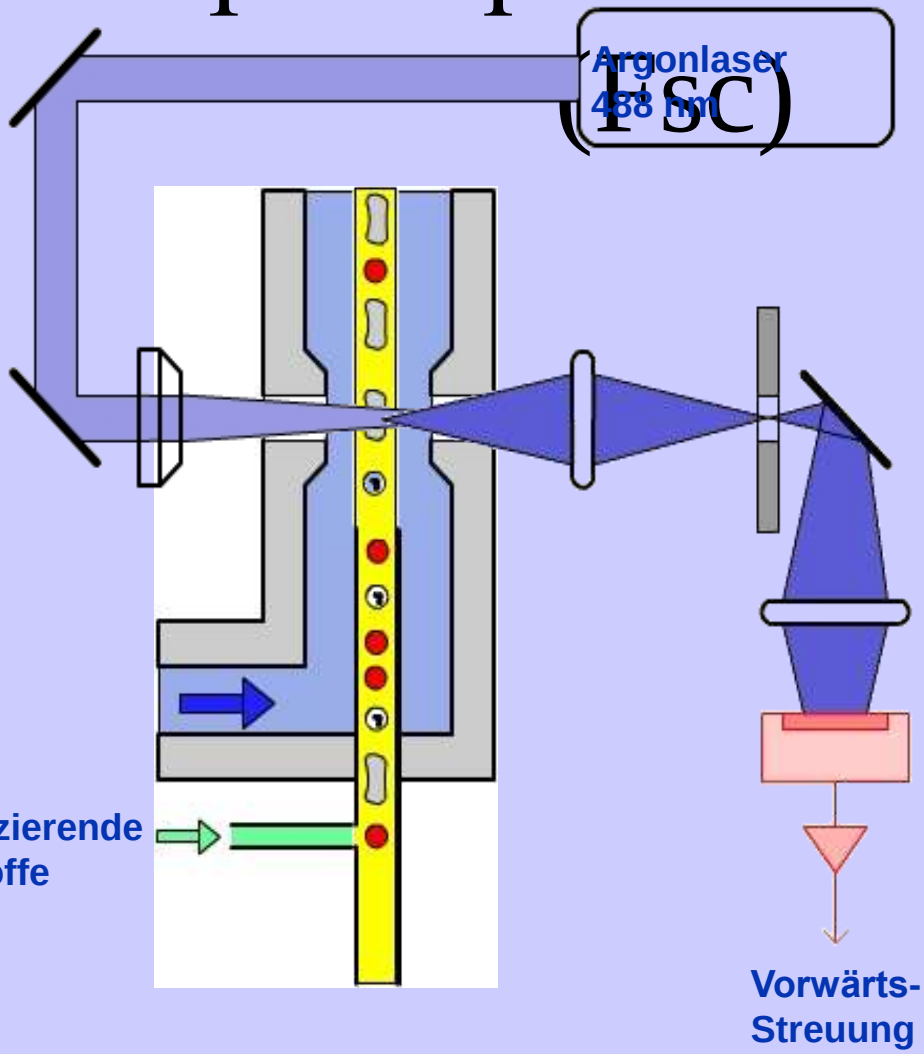
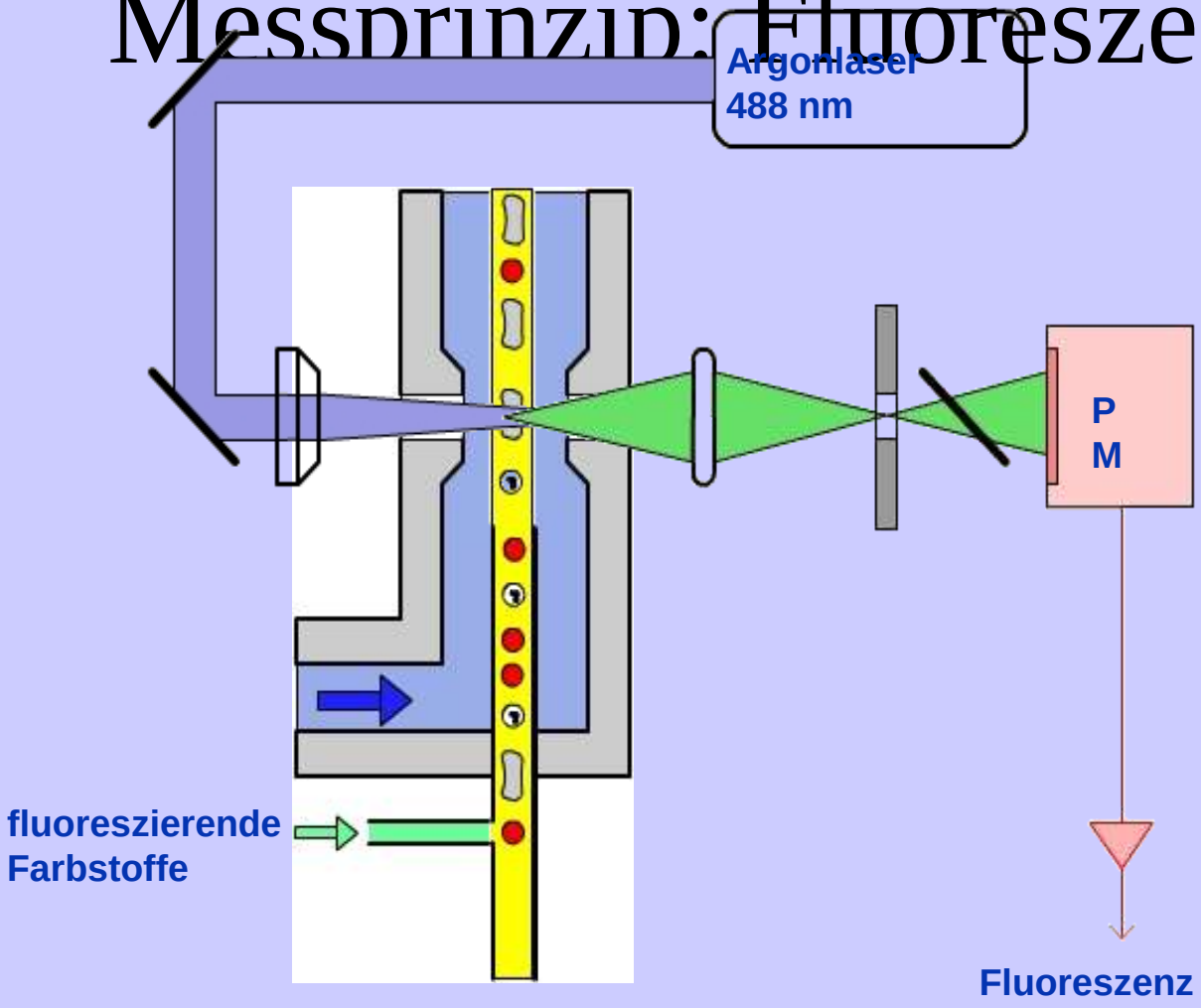
Messprinzip: Vorwärtsstreung (FSC)



Messprinzip: Fluoreszenz (Fl)

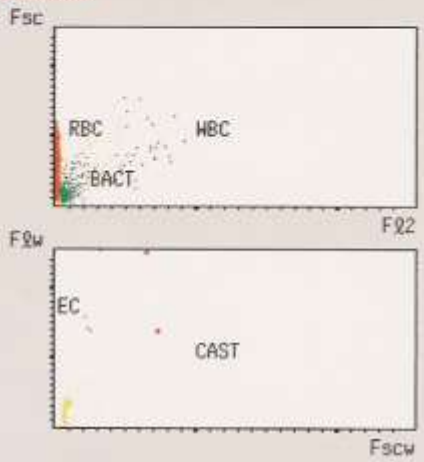


RBC① (Glomerular)

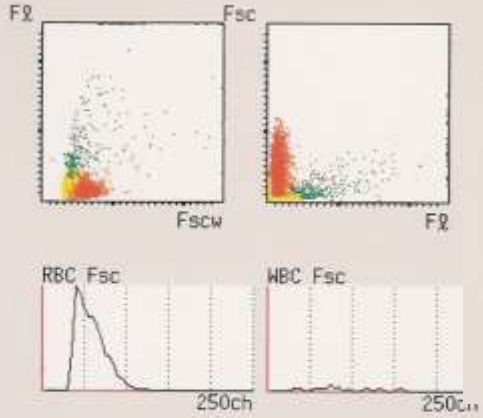
UF-100 Scattergram

Scattergram on main display

REVIEW



Scattergram on second page



RBC	1325.1+ [/μL]	238.5[/HPF]
HBC	9.8 [/μL]	1.8[/HPF]
EC	1.8 [/μL]	0.3[/HPF]
CAST	0.26+ [/μL]	0.74[/LPF]
BACT	82.0 [/μL]	14.8[/HPF]

Path.CAST +	X'TAL
SRC	SPERM
YLC	

RBC-Info. Dysmorphic ?

OB/Hb 3+	PRO 3+
L.Est. –	NIT –

Dipstick Data

Glucose (–)	Bilirubin (–)	Ketone (–)	Specific gravity (1.020)
Occult blood (3+)	pH (5.0)	Protein (3+)	Urobilinogen (0.1)*
Nitrite (–)	WBC Esterase (–)		

*Ehrlich unit /dl (Normal reference value : 0.1/dl ≧)

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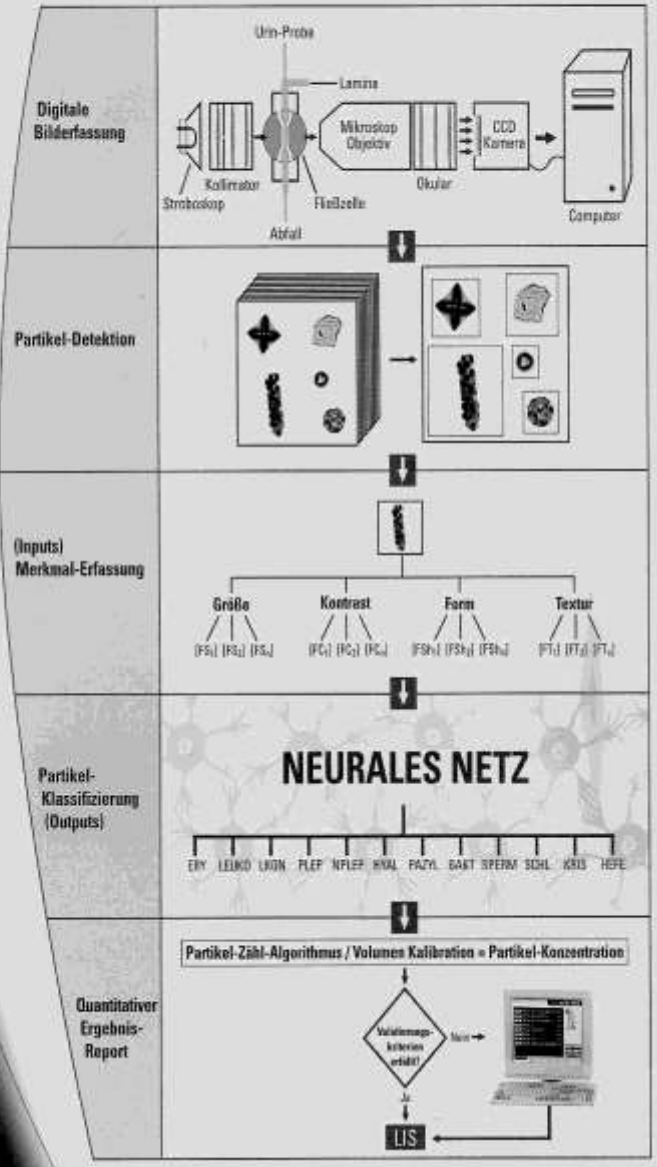
automatisiertes
Urin-Mikroskop-Analysesystem

Instrumentation Laboratory

W. Hofmann, munich

iQ®200 - innovative vollautomatische Urin-Partikel-Mikroskopie für Ihr Labor

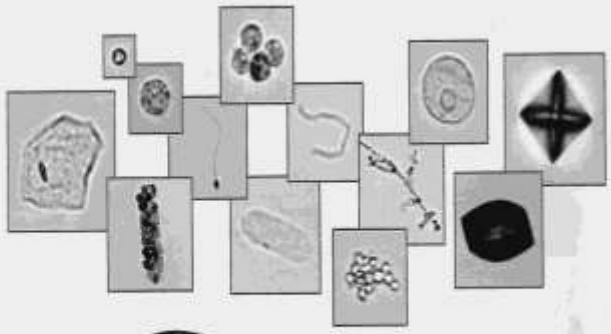
Analyse-Prozess



Auto-Particle Recognition (APR™)

Die in der Probe vorhandenen Urin-Partikel werden mit Hilfe einer neuartigen, speziellen **Muster-Erkennungs-Software** unter Verwendung eines neuralen Netzwerkes in verschiedene Hauptgruppen klassifiziert (Erythrozyten, Leukozyten, Leukozytenkonglomerate, Bakterien, Hefen, hyaline und pathologische Zylinder, Plattenepithelien und Nicht-Plattenepithelien, Kristalle, Sperma und Schleimfäden). Die Ergebnisse werden qualitativ bzw. quantitativ ausgegeben. Die Photos aller in der Probe gefundenen Partikel werden auf dem Bildschirm angezeigt. Das neurale Netzwerk basiert auf einer Datenbank, die aus mehr als 26.000 Partikelbildern besteht.

Beispielbilder der 12 Hauptklassen, wie sie vom iQ 200 angezeigt werden.



innovativ

- standardisierte Methode, die objektive und reproduzierbare Ergebnisse liefert
- akurate Klassifizierung und Quantifizierung von zwölf verschiedenen Urin-Partikeln
- deutlich erkennbare Photos der Urin-Partikel - keine Scattergramme

Probenbe

produktiv

- Naïe-Urin - keine zeitaufwendige Probenvorbehandlung
- Racksystem mit kontinuierlicher Probenbeladung
- automatische Ergebnisfreigabe und / oder wahlweise Überprüfung am Bildschirm
- Archivierung der Ergebnisse und Mikroskop-Photos
- Option zur weiteren Unterklassifizierung der Urin-Partikel

START

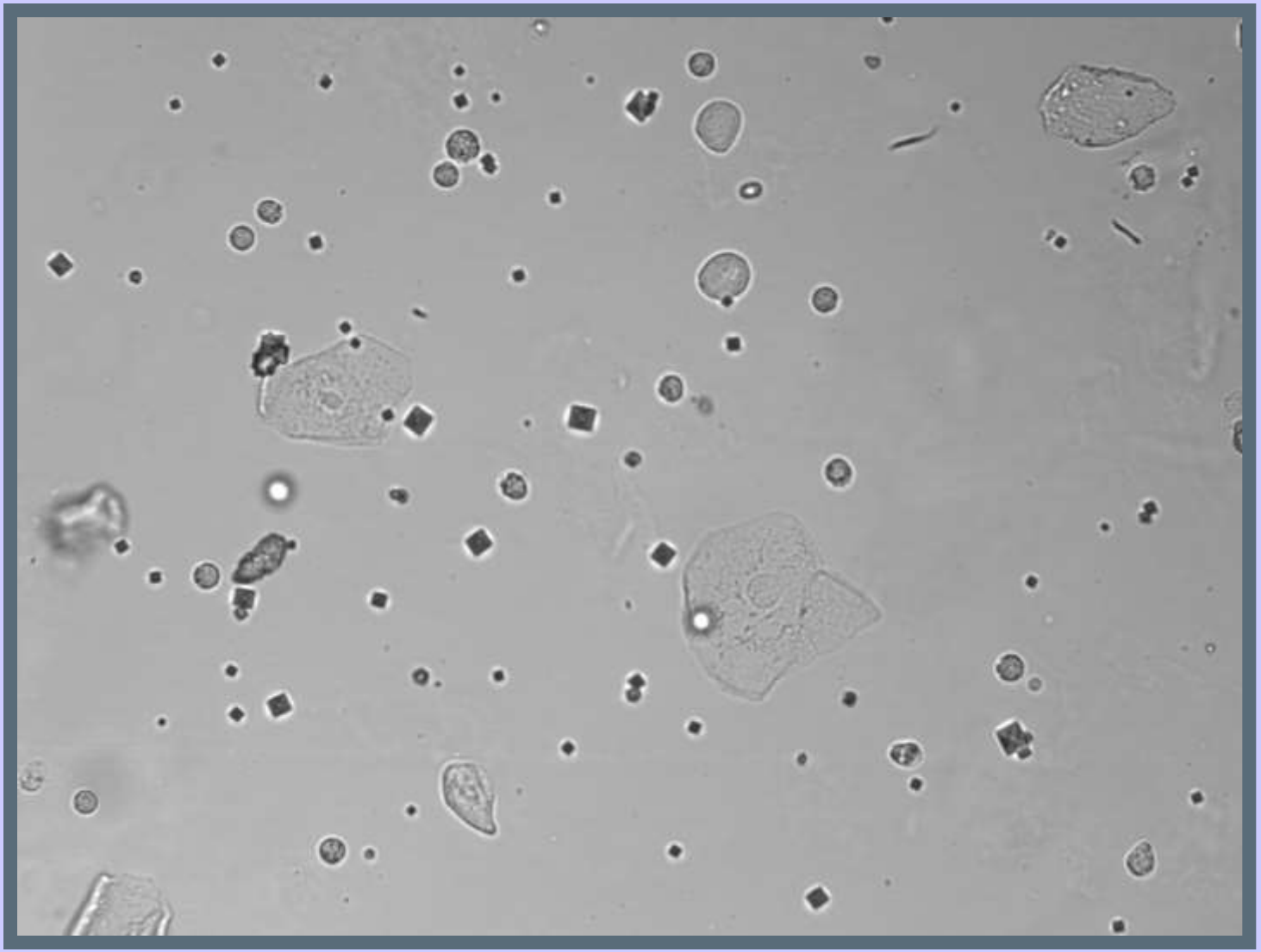
einfach und schnell

- Walk-away System - ca. 80 Proben / Stunde
- signifikante Zeitersparnis
- Kosteneffektivität bei unterschiedlichsten Probenaufkommen
- einfache Bedienung und Wartung

sediMAX

A.MENARINI diagnostics

Das sehen Sie:
WBC, NEC, EPI, CaOxd



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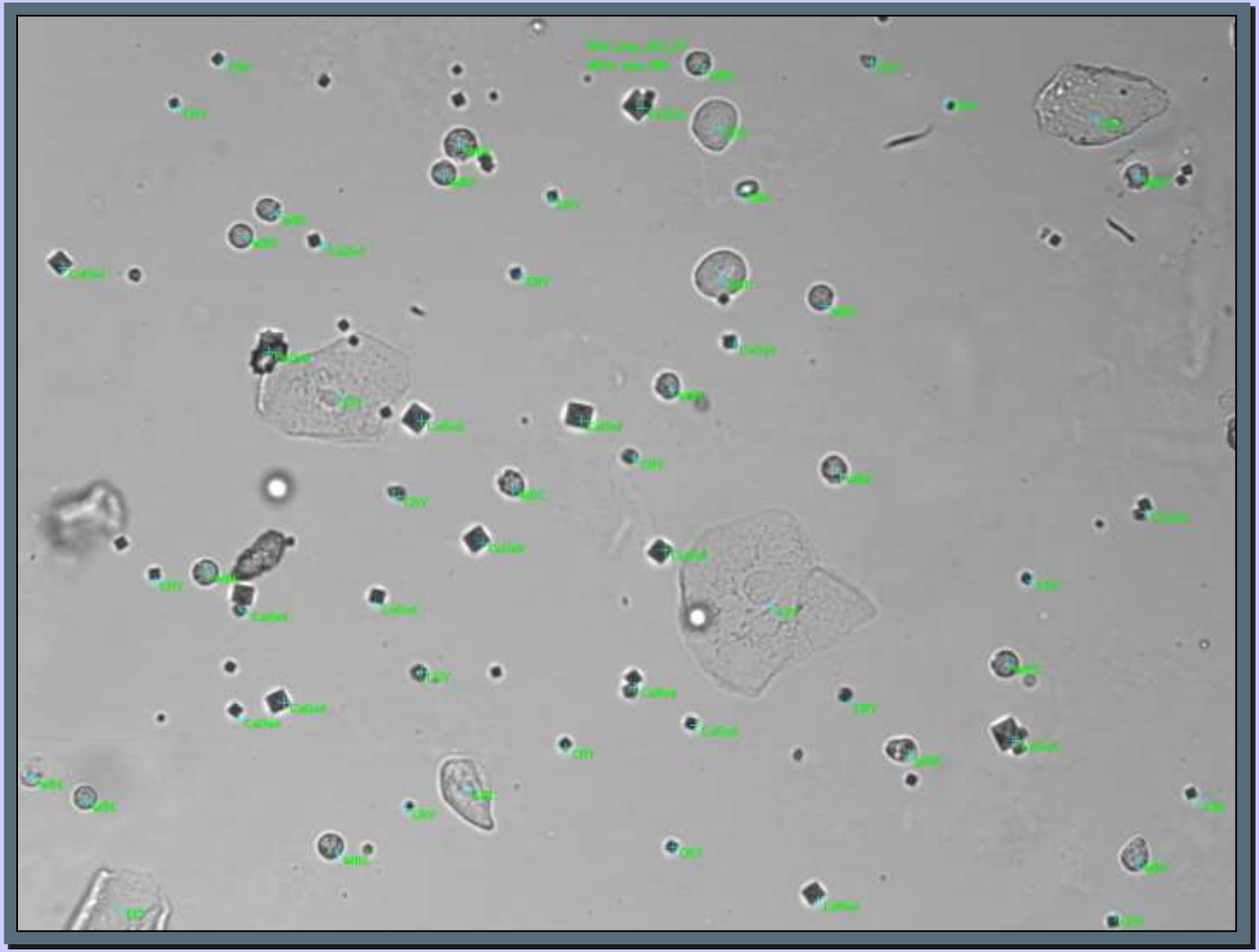
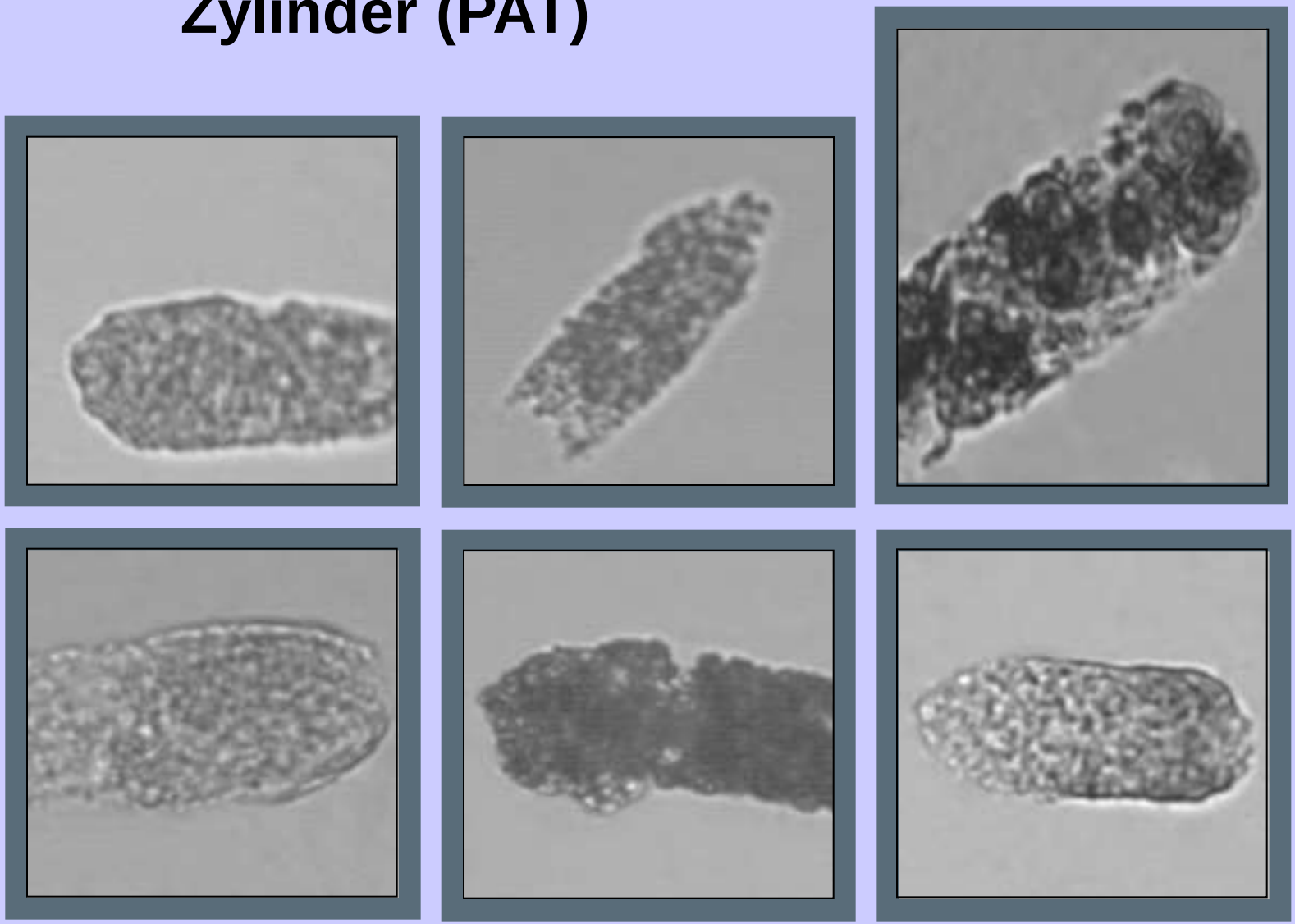
Und das macht sedi*MAX* daraus



Beispiele nachgewiesener Partikel IV
Zylinder (PAT)



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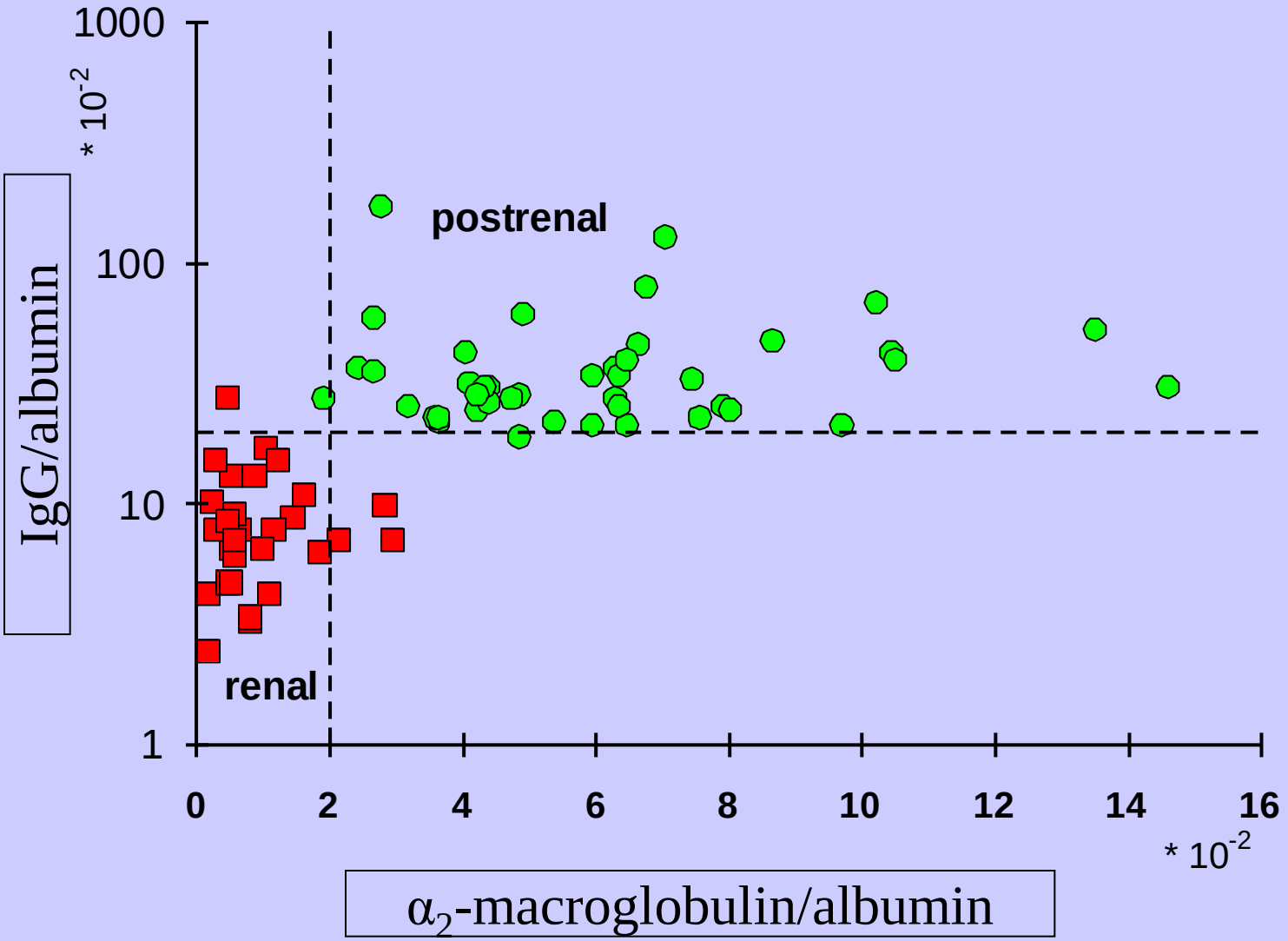
Type of hematuria



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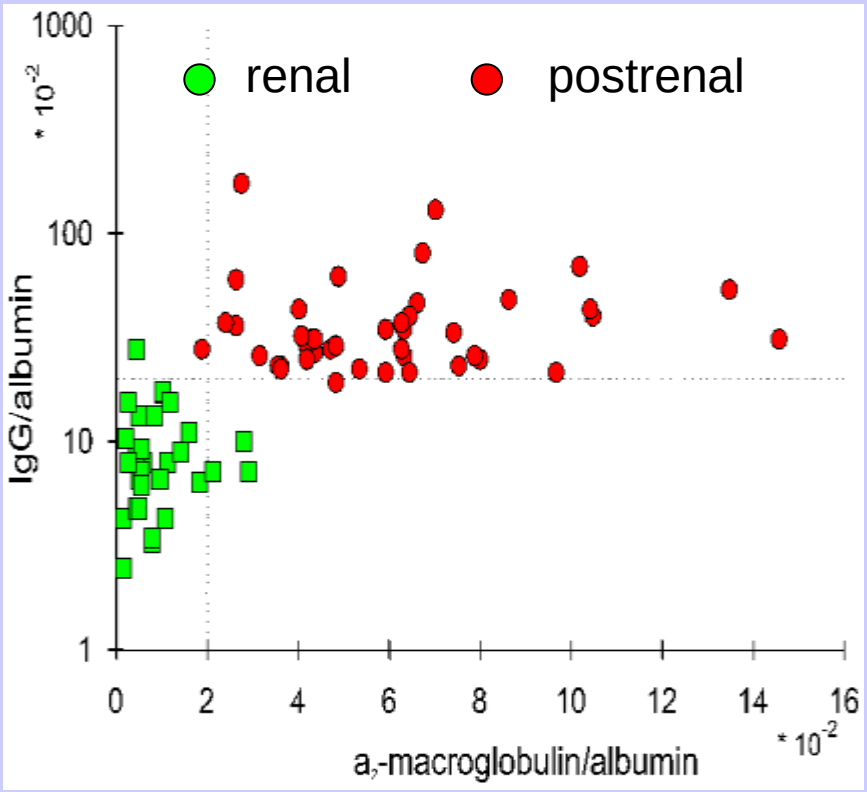
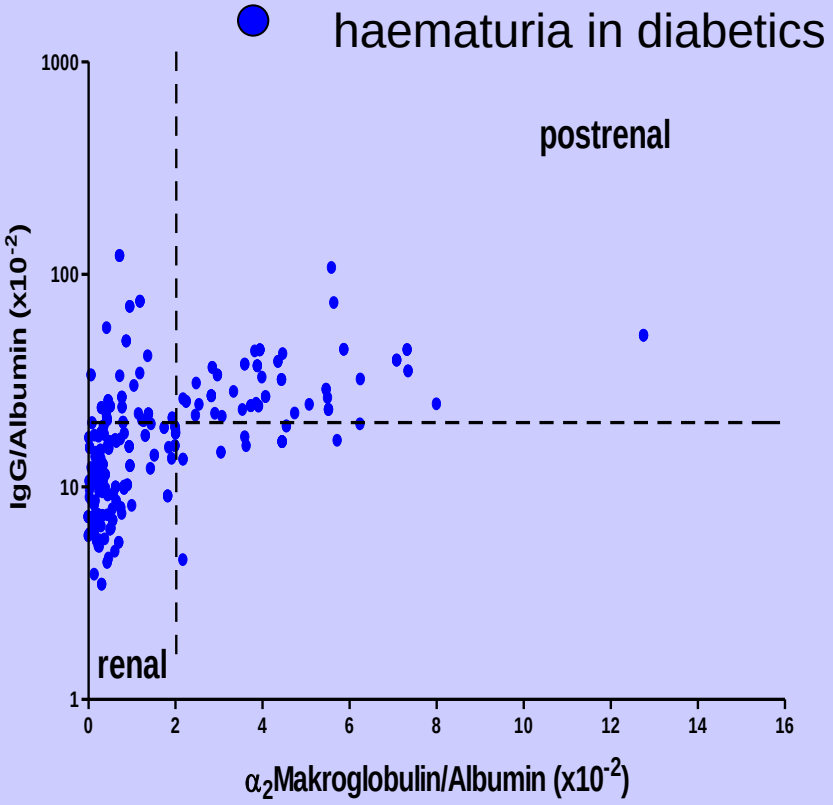
Differentiation of haematuria by urine protein pattern analysis





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The European Urinalysis Group

Timo Kouri - Chair/Chemistry/Quality

Walter Guder - Chemistry/Strategy

Walter Hofmann - Chemistry

Giovanni Fogazzi - Microscopy/Nephrology

Vanya Gant - Secretary/Microbiology

Hans Hallander - Microbiology

The new knowledge and technology has been included into a recently appearing European Guideline of Urinalysis whose members came from nephrology, microbiology and clinical chemistry supported by 50 corresponding members from all European countries and the diagnostic industry.

Diagnostic Pathways

Working group Kidney

- Prof. Dr. F. Keller (GfN)
- Prof. Dr. J. Scherberich (GfN)
- Prof. Dr. H. Ehrich (GfN) (seit 2008)
- Prof. Dr. W.G. Guder (DGKL)
- Prof. Dr. W. Hofmann (DGKL)

1. Session 1. Oktober 2007/München
2. Session 30. November 2007/München
3. Session 29. Februar 2008/München
4. Session 03. April 2008/München
5. Session am 17. April 2008/München

Clin. Lab. 2012;58:XXX-XXX

REVIEW ARTICLE

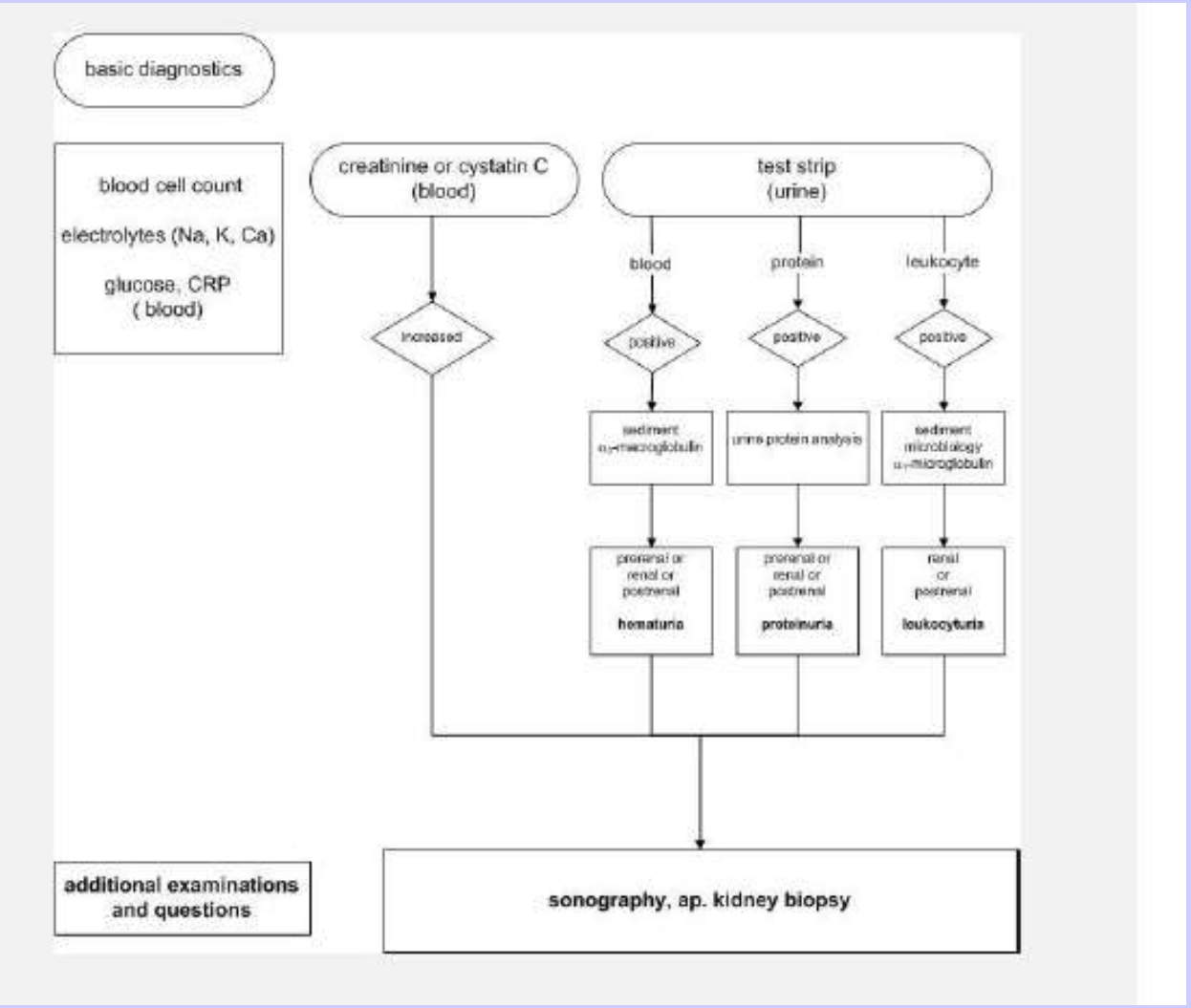
Diagnostic Pathways for Exclusion and Diagnosis of Kidney Diseases

WALTER HOFMANN [1], JOCHEN H.H. EHRICH [2], WALTER G. GUDER [1], FRIEDER KELLER [3], JÜRGEN SCHERBERICH [4]

Working Group Diagnostic Pathways of the German United Society for Clinical Chemistry and Laboratory Medicine and the Society of Nephrology

[1] *Department of Clinical Chemistry, Community Hospital Munich GmbH, Munich, Germany*
[2] *Department Pediatric Kidney, Liver and Metabolic Diseases, Medical University, Hannover, Germany*
[3] *Department Nephrology, Department Internal Medicine 1, University Clinic, Ulm, Germany*
[4] *Clinic for Kidney- & Hypertension Diseases - Clinical Immunology, Community Hospital Munich GmbH, Munich, Germany*

DIAGNOSTIC PATHWAYS FOR EXCLUSION AND DIAGNOSIS OF KIDNEY DISEASE



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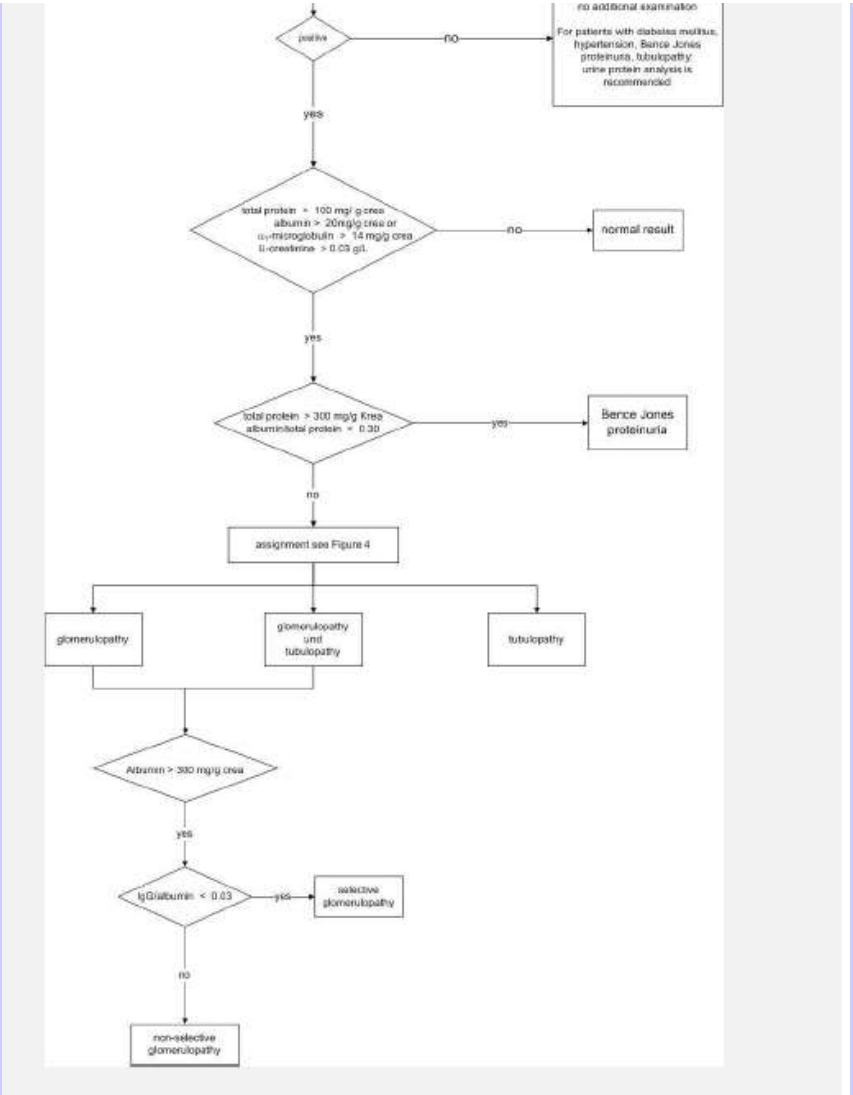
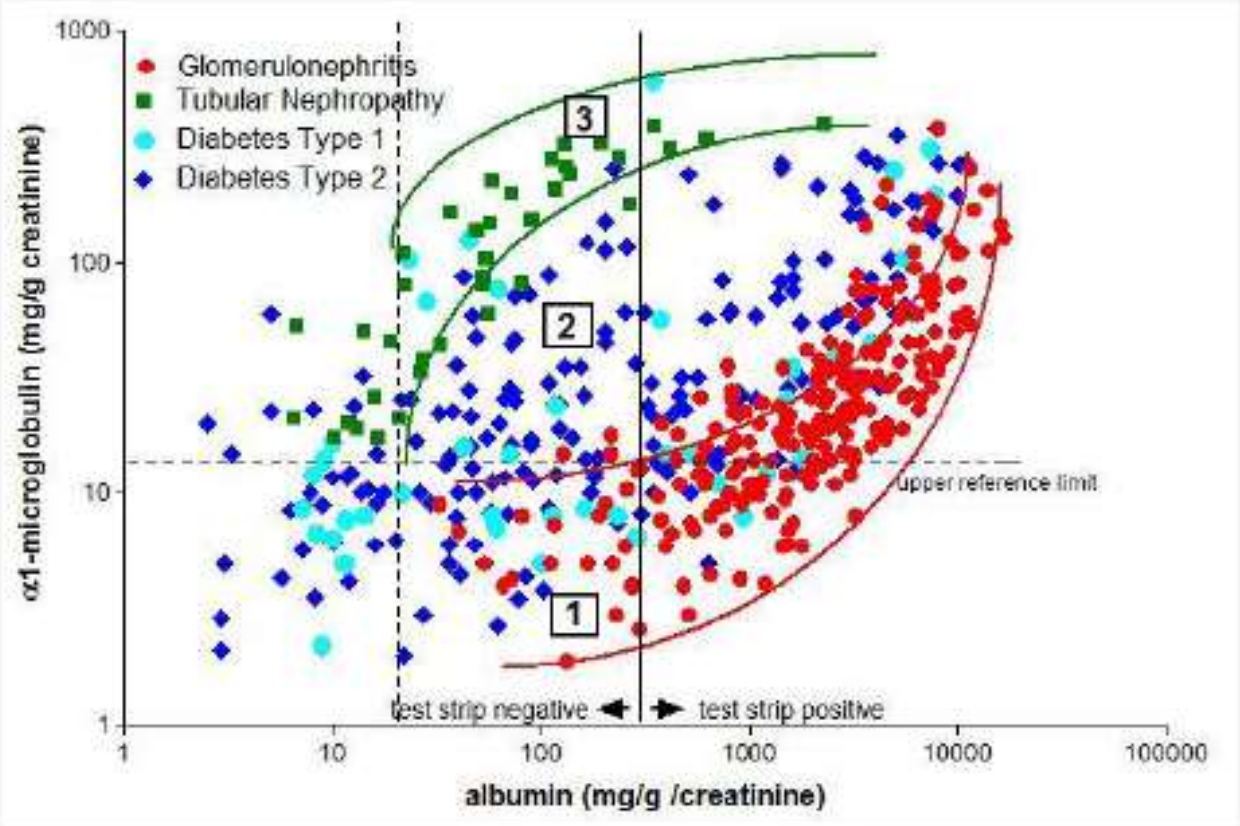
DIAGNOSTIC PATHWAYS FOR EXCLUSION AND DIAGNOSIS OF KIDNEY DISEASE



DIAGNOSTIC PATHWAYS FOR EXCLUSION AND DIAGNOSIS OF KIDNEY DISEASE



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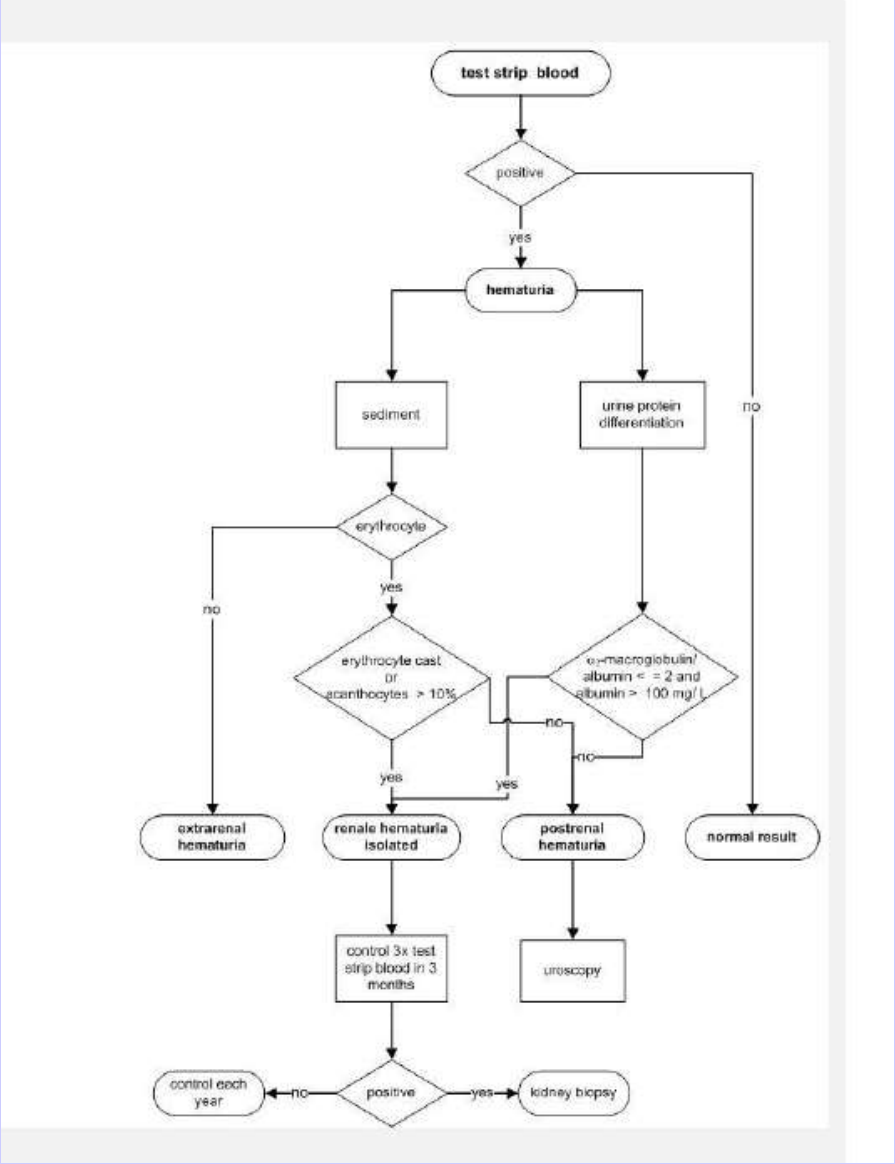
DIAGNOSTIC PATHWAYS FOR EXCLUSION AND DIAGNOSIS OF KIDNEY DISEASE



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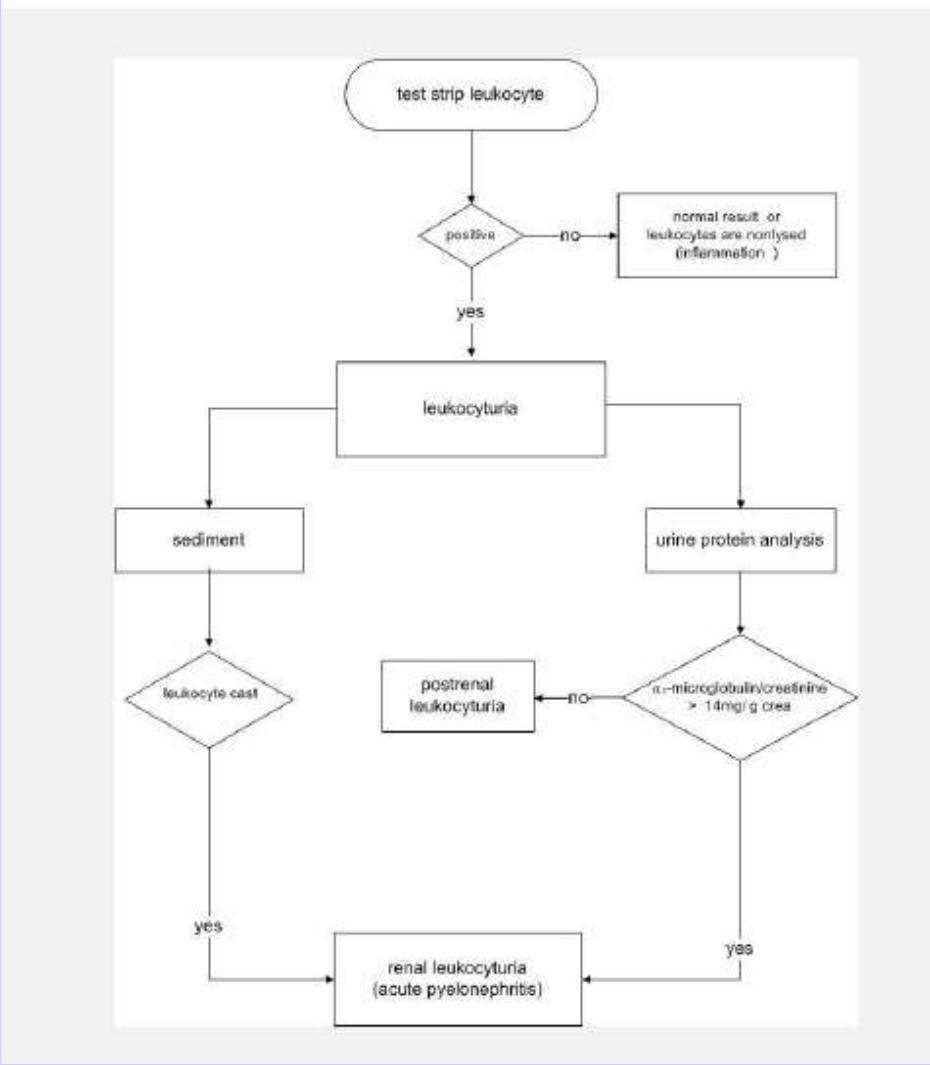
DIAGNOSTIC PATHWAYS FOR EXCLUSION AND DIAGNOSIS OF KIDNEY DISEASE



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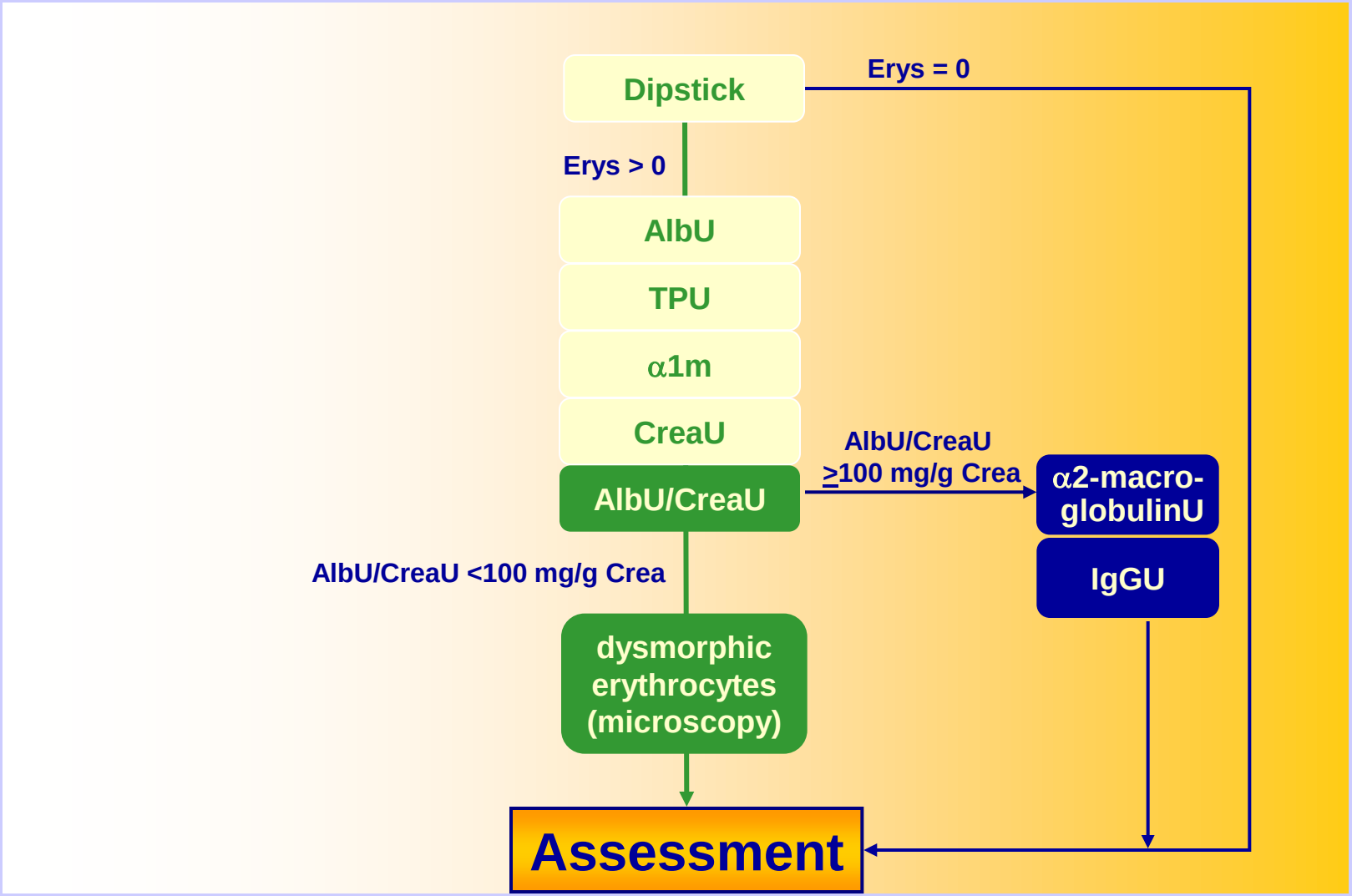
Protis

3: Hematuria Assessment



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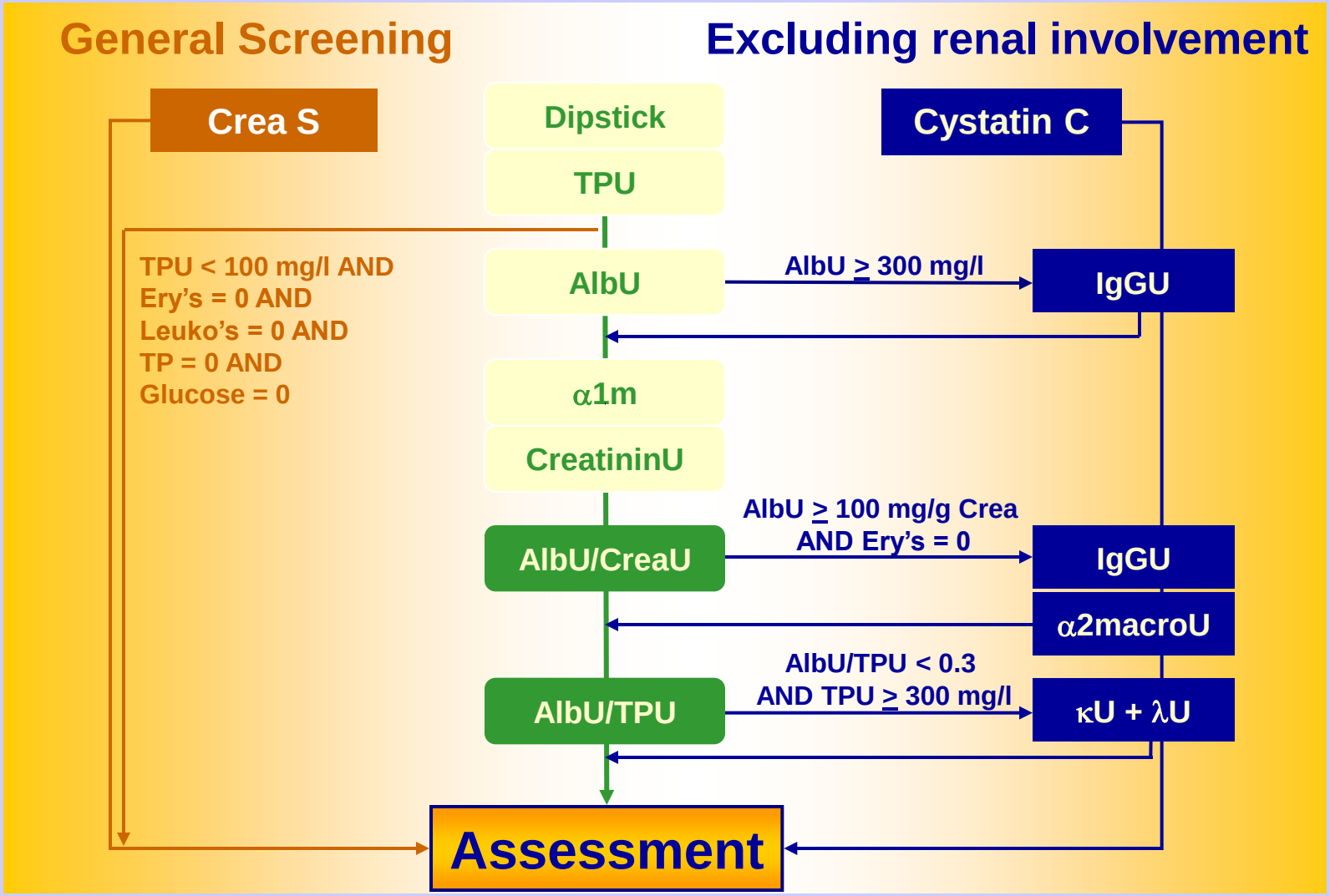
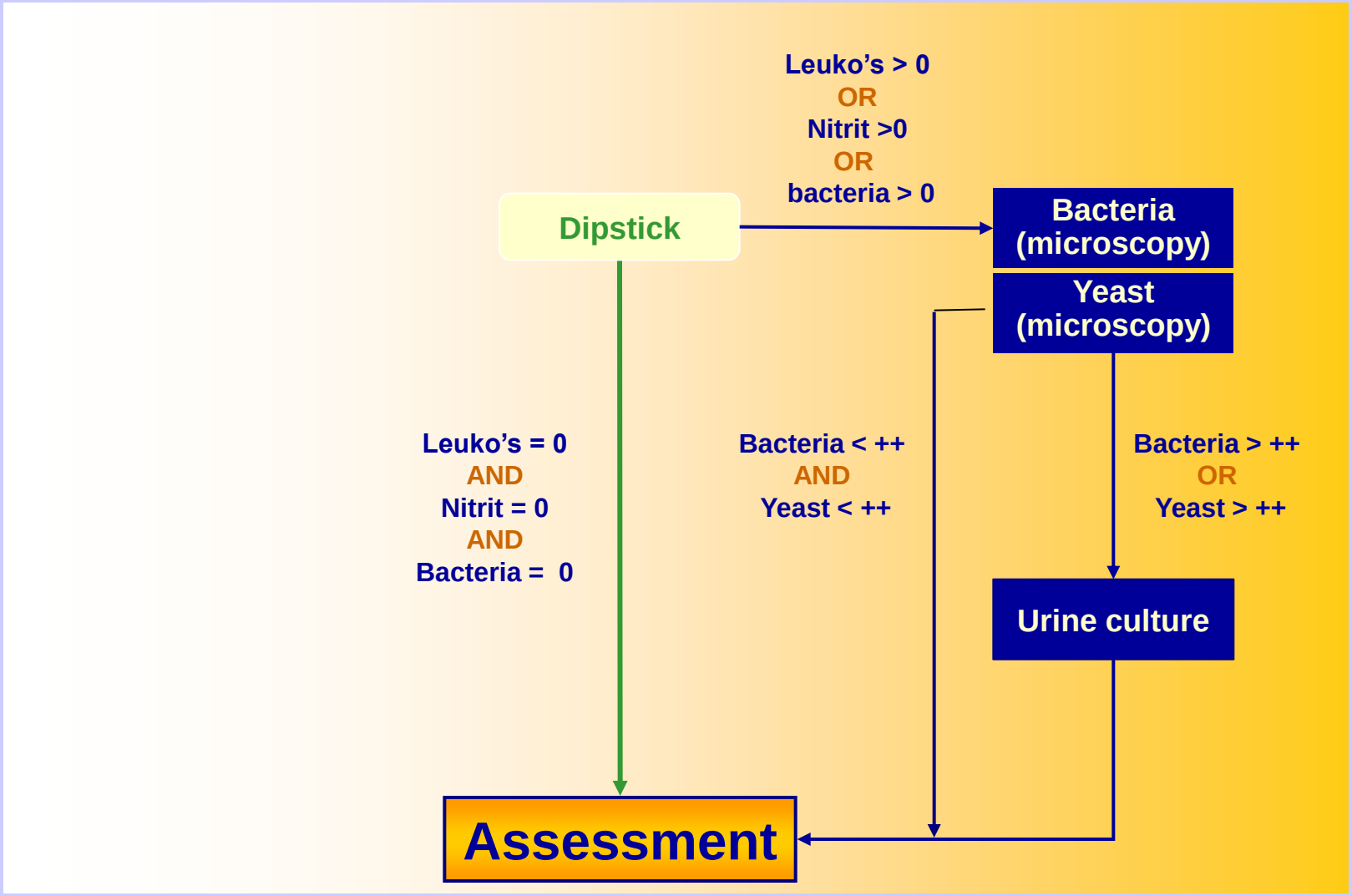
1 and 2: Proteinuria Differentiation

Protis



Protis

4: Urinary Tract Infection



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Thank you for your attention

分析方法

可以设想
蛋白尿的
可选方法
均作了检
还有试纸
作，象潜

目前的检

1
2
3
4
5. N-乙酰-β-右旋-葡糖胺甙酶作为近段肾小管细胞的酶标

此外，也测定肌酐以及总蛋白，作为诊断肾后性蛋白尿的辅助指标。

临床应用

这种新的检测方法已经与试纸法及尿沉渣分析一起，应用于如下几点：

1. 排除肾脏疾病
2. 糖尿病性肾病的早期诊断以及对疑有此病者进行监测。
3. 鉴别肾小球性及肾小管性肾脏疾病
4. 鉴别肾性和肾后性血尿

1. 在普查中证实，尿蛋白的定量分析比过去沿用的方法明显敏感。新发异常结果中大部分是低于试纸法检出阈值之下的肾小球蛋白尿及肾小管蛋白尿(参考文献4)。由此得出结论，用于排除有临床意义的肾脏疾病，只需测定白蛋白和α1-微球蛋白，同时用试纸法检测血红蛋白和白细胞即可。为发现本-周氏蛋白尿，可以采用白蛋白与蛋白总量的比例(白蛋白/总蛋白≤0.3)，也可用抗κ链和λ链的综合性抗体来替代(参考文献5)。

2. 诸多的临床和流行病学研究表明，用敏感方法可以检出“微白蛋白尿”，据此可以采取措施滞缓糖尿病肾病的发展过程，即使不被完全阻止的话。根据我们的经验，在对糖尿病进行了稳定的代谢调节后的首次检查中，值得推荐检测白蛋白、α1-微球蛋白以及必要时α2-巨球蛋白，以排除肾性及肾后性的疾病。只有在排除了肾间质性和肾后性疾病之后，才能将微白蛋白尿视为

ANALYTICAL METHODS

ify
te-
of
nd
In
ic.

1. Albumin to assess glomerular function
2. α1-microglobulin as marker of tubular protein reabsorption
3. IgG as inflammation and selectivity marker
4. α2-macroglobulin as marker of postrenal bleedings
5. N-Acetyl-ß-D-Glucosaminidase as enzymic marker of tubular cells

In addition creatinine is determined to measure renal concentration and total protein to detect prerenal proteinurias (2).

Protein Differentiation Text

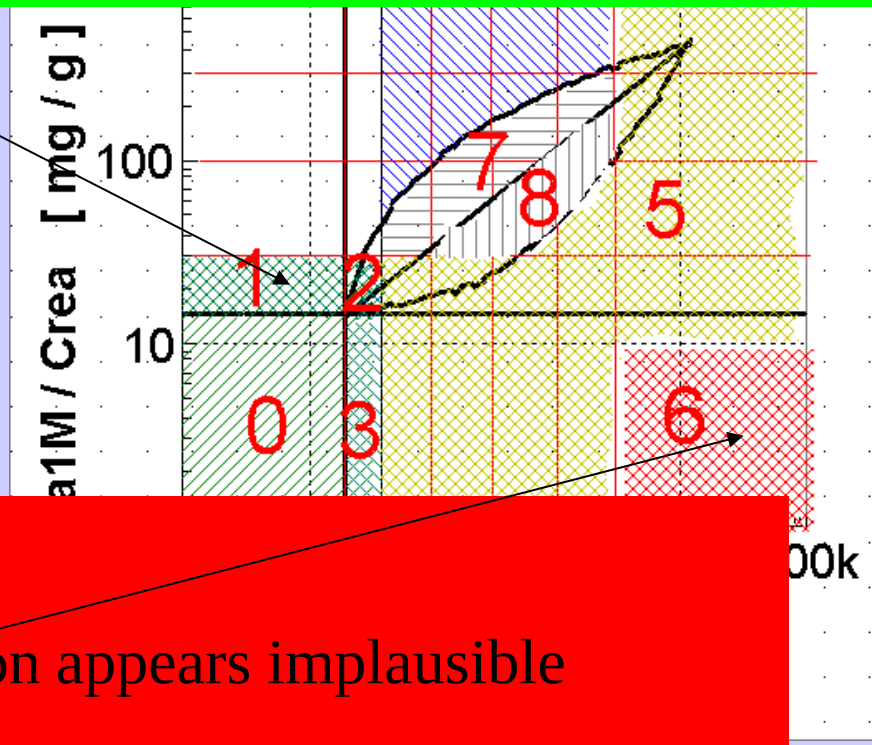
Protis

1

This constellation is compatible with tubulo-interstitial dysfunction.

tbsProtDysInt

Condition		
1		
3		
2		
0 and CreaS>2.		
4		
5	This constellation is compatible with primary or secondary glomerulopathy. (e.g. glomerulonephritis, diabetic or hypertensive nephropathy).	tbsProtGN & " & tbsProtGNBsp
Consideration of of a1M-corrected		
5 a1korr<14 and a1M path.	Increased excretion of the tubular marker alpha1 microglobulin is attributable to overflow proteinuria (exhaustion of tubular reabsorption capacity with albuminuria > 3 g/g creatinine).	tbsProta1Over
5 a1korr<14 and a1M normal	There is no indication of restricted tubulo-interstitial reabsorption.	tbsProtGNOhneInt
5 a1korr>14	Borderline restriction of tubulo-interstital reabsorption is simultaneously found.	tbsProtGNStufenInt1
5 a1korr>20	Slight restriction of tubulo-interstital reabsorption is simultaneously found.	tbsProtGNStufenInt2
5 a1korr>50	Significant restriction of tubulo-interstital reabsorption is simultaneously found.	tbsProtGNStufenInt3
5 a1korr>100	Distinct restriction of tubulo-interstital reabsorption is simultaneously found.	tbsProtGNStufenInt4
8	This constellation is compatible with glomerulopathy with restricted tubulo-interstitial reabsorption.	tbsProtGNInt
7	This constellation is compatible with interstitial nephropathy	tbsProtIntGN
Discriminat		
7and no intertitial glomerular i		
7 and intertitial but glomerular i		
intertitial but glomerular i		
6		



6

This marker protein constellation appears implausible

tbsProtUnplaus

UPESA03

Haematuria Text

Protis

Condition	Text	Text ID
alpha2 forgotten to measure	Differentiation of hematuria is only possible if alpha2 macroglobulin and albumin have been measured or by means of phase contrast microscopy!	tbsBlut0
Alb <100 mg/l Hematuria Differentiation not possible No Point in Diagram	Differentiation of renal and postrenal hematuria is impossible at albumin concentrations < 100 mg/l using protein analysis. Phase contrast microscopy of a fresh first morning urine may allow to distinguish renal from postrenal causes of hematuria (acanthocytes?).	tbsBlutAlb100
Point within the right down filed of the Diagram	The hematuria differentiation marker proteins (alpha2 macroglobulin, IgG) do not allow clear interpretation. Phase contrast microscopy (fresh, first morning urine, acanthocytes?) may enable the distinction of renal and postrenal hematuria. In the case of postrenal hematuria, urine protein differentiation is recommended following abatement.	tbsBlutFrag
Diagram shows post renal Hematuria	The presence of postrenal hematuria is highly likely; the excretion of renal and postrenal proteins cannot be distinguished.	tbsBlutPost
Diagram shows post renal Hematuria and Dipstick Leukocytes>0	Leucocyturia and, with a high degree of probability, postrenal hematuria, is present; the excretion of renal and postrenal proteins cannot be distinguished.	tbsBlutPostLeuk
Diagram shows renal Hematuria	The presence of renal hematuria is highly likely; additional erythrocytes from postrenal sources cannot be ruled out.	tbsBlutRenal1
a2M/Alb<0,02 but IgG/Alb>0,2	The presence of renal hematuria is likely; phase contrast microscopy (fresh, first morning urine, acanthocytes?) should additionally be used to confirm this.	tbsBlutRenal2
Discussion of a1M		
post renal indication	Control is recommended following the abatement of the hematuria.	tbsBlutWh

a2M/Alb<0,02 but IgG/Alb>0,2

The presence of renal haematuria is likely; phase contrast microscopy (fresh, first morning urine, acanthocytes?) should additionally be used to confirm this.