尿液檢驗現況檢討與CKD慢性腎病篩檢之推廣

臨床體液鏡檢概述

國立臺灣大學　工學院 醫學工程學研究所
醫學院 附設醫院檢醫部
朱蘇煜

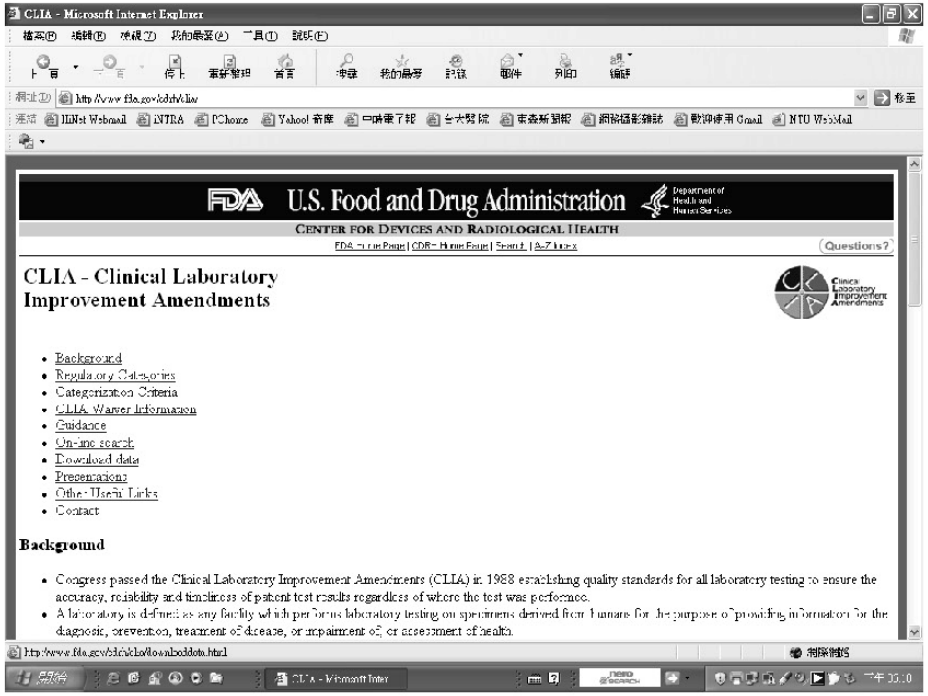
2010.11.28

BioNEMS
Medical Micro-Sensors and Systems Laboratory
National Taiwan University
Institute of Biomedical Engineering
Institute of Applied Mechanics
Graduate Institute of Biomedical Electronics and Bioinformatics
Center for Advanced Nano-Matericals

美國 現今對於CKD的篩檢方法

- Food and Drug Administration, FDA.

  Clinical Laboratory Improvement Amendments :
  CLIA 67' and 88'



Federal Law
No License, No test.

February 2002,
Kidney Disease Outcomes Quality Initiative (K/DOQI)
of the National Kidney Foundation (NKF)

Definition : Chronic Kideny Disease (CKD)

- Kidney damage or Decreased kidney function for 3 Months

  1. Persistent proteinuria.
  2. Albumin-creatinine ratio greater than 30 mg/g in spot urine.
  3. Other markers of damage, abnormalities in urine sediment, blood, and urine chemistry measurements.
  4. Abnormal findings on imaging studies.

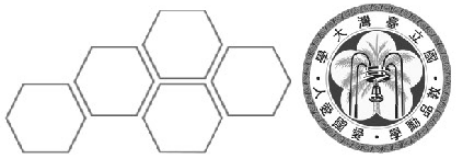
Assessment of proteinuria for CKD by Dipstick

- First morning spot urine is prefered. Avoiding orthstatic proteinuria.

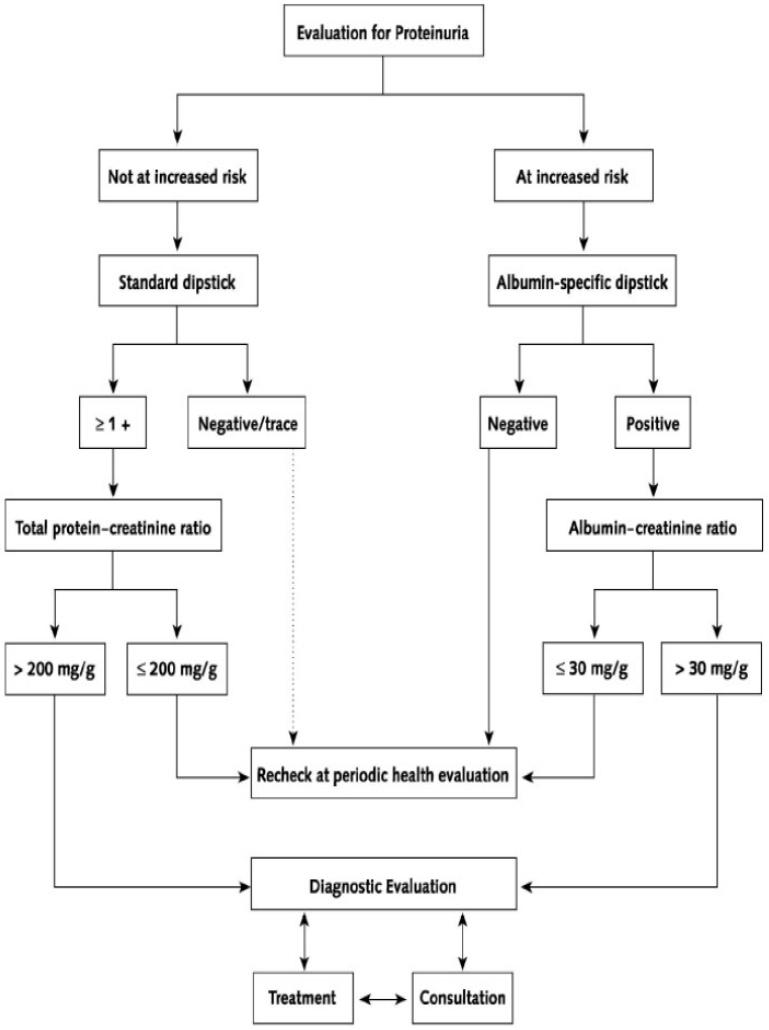
- Dipstick is low cost and convenient.
  Standard dipstick
  Protein-to-creatinine or Albumin-to-creatinine.

- Children
  No diabetes : Standard dipstick or Protein-to-creatinine
  Diabetes : Post-pubertal children, 5 years, Albumin-to-creatinine
  Other : Standard dipstick or Protein-to-creatinine

- Adult
  Not at risk : Standard dipstick or albumin-to-creatinine
  At risk : Albumin-to-creatinine
  Albuminuria ＞500-1000 mg/g →
  Total protein-to-creatinine



National Kidney Foundation Practice Guidelines for Chronic Kidney Disease:



Ann Intern *Med.* 2003;139:137-147.

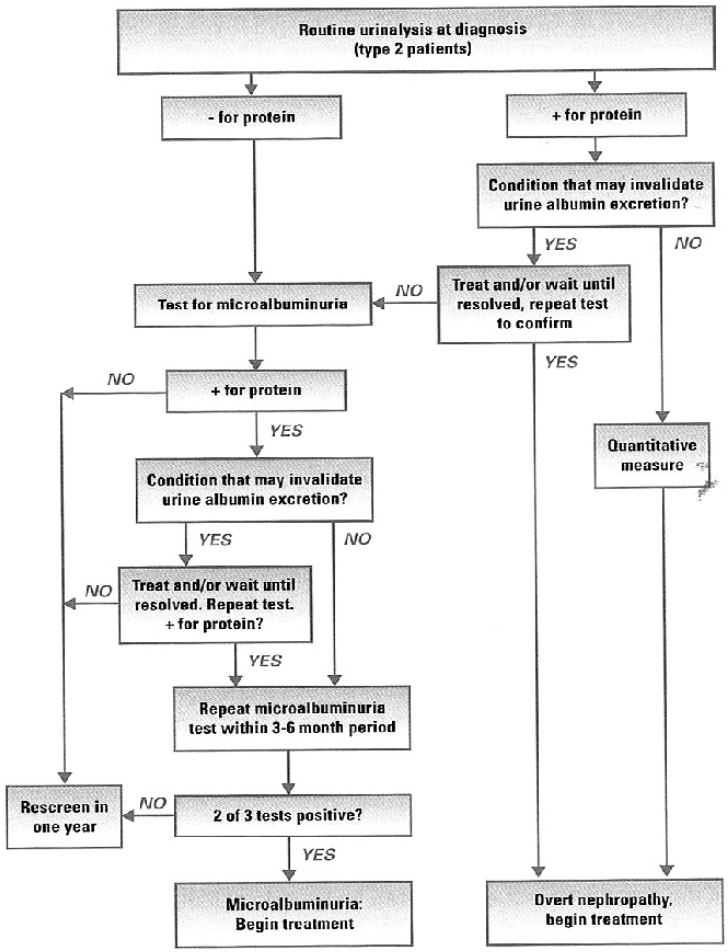


Figure 4. A flow chart by the American Diabetes Association that can be used as a guide to microalbuminuria testing.

Comparison and Interpretation of Urinalysis Performed by a Nephrologist Versus a Hospital-Based Clinical Laboratory

Jason J. Tsai, MD, Jane Y. Yeun, MD, Victoria A. Kumar, MD, and Burl R. Don, MD

• *Background:* Urinalysis (UA) is considered the most important laboratory test in evaluating patients with kidney disease. Anecdotally, we have observed differences between results of UA performed by nephrologists compared with those performed by certified medical technologists or clinical laboratory scientists that could affect a clinician's diagnosis. Whether there are differences between UA performed by the clinical laboratory and that performed by a nephrologist was determined, and accuracy of diagnosis based on interpretation of the UA was compared. *Methods:* Urine samples were obtained from 26 patients with acute renal failure (ARF). An aliquot of urine was sent to the clinical laboratory for UA. Nephrologist A, blinded to the patient's clinical information, performed a UA on the other aliquot of urine, generated a report, and assigned the most likely diagnosis for ARF based on UA findings. Nephrologist B, also blinded to the clinical information, reviewed nephrologist A's UA reports and assigned a diagnosis for ARF to each report. Nephrologists A and B both assigned a diagnosis (or diagnoses) for the ARF based on laboratory UA results. These 4 sets of diagnoses were compared with those assigned by the consult nephrologists. *Results:* Nephrologist A correctly diagnosed the cause of ARF in 24 of 26 samples (92.3% success rate) based on his performance of the UA. Diagnoses by nephrologists A and B, based on their review of the clinical laboratory UA report, were correct in only 23.1% and 19.2% of the samples, respectively. Accuracy of diagnosis for nephrologist B improved to 69.3% when she reviewed UA reports from nephrologist A. Nephrologist A's review of urine sediment was significantly more accurate than interpretations by nephrologist A or B of clinical laboratory reports (sign test, $P < 0.001$). Nephrologist A reported a greater number of renal tubular epithelial (RTE) cells ($P < 0.0001$), granular casts ($P = 0.0017$), hyaline casts ($P = 0.0233$), RTE casts ($P = 0.0008$), and dysmorphic red blood cells. The laboratory noted a greater number of squamous cells ($P = 0.0034$). *Conclusion:* A nephrologist is more likely to recognize the presence of RTE cells, granular casts, RTE casts, and dysmorphic red blood cells in urine. The laboratory may be reporting RTE cells incorrectly as squamous epithelial cells. Nephrologist-performed UA is superior to laboratory-performed UA in determining the correct diagnosis. *Am J Kidney Dis* 46:820-829.

INDEX WORDS: Urinalysis; clinical laboratory; acute renal failure.

URINALYSIS (UA) is the first and most important laboratory test in evaluating a patient with suspected kidney disease.[1-7] In the past, both clinicians and laboratory technologists have performed macroscopic (direct observation of physical characteristics and chemical dipstick testing) and microscopic examination of urine. Recently, there has been much greater reliance on the clinical laboratory and medical technologists for performance of UA, in part because of implementation of Clinical Laboratory Improvement Amendments (CLIA) of 1988.[8] Because CLIA mandates that most laboratory tests be performed by CLIA-certified personnel, who are usually technologists, UA performance is becoming a dying art among clinicians,[9] and many physicians have not been adequately trained to perform urine microscopy.[10]

In our medical center, nephrologists and nephrologists in training perform the UA when a consultation for renal disease is requested. However, non-nephrologists frequently rely on the clinical laboratory to perform the UA. Anecdotally, we have observed major differences between the nephrologist and clinical laboratory evaluations of urinary sediment of a given patient that could affect the clinical diagnosis. The purpose of this study is to test the hypothesis that such differences exist and determine which UA evaluation and subsequent interpretation leads to the most accurate clinical diagnosis.

METHODS

Twenty-six patients admitted to the University of California Davis Medical Center (Sacramento, CA) between Sep-

From the Division of Nephrology, University of California Davis Medical Center, Sacramento, CA.

Received February 1, 2005; accepted in revised form July 11, 2005.

Originally published online as doi:10.1053/j.ajkd.2005.07.039 on October 4, 2005.

Address reprint requests to Burl R. Don, MD, Division of Nephrology, University of California Davis Medical Center, 4150 V St, Ste 3500, Sacramento, CA 95817. E-mail: brdon@ucdmc.ucdavis.edu

0272-6386/05/4605-0004$30.00/0

doi:10.1053/j.ajkd.2005.07.039

Subject:

UCLA Davis,200109-200203, 26 ARF patient.

Result:

Dr. A / Dr.A	24/26	92.%
Dr. A / Dr. B	?/26	?%
Dr. A / Lab	6/26	23%
Dr. B / Dr. A	18/26	69.3%
Dr. B / Lab	5/26	19.2%

Conclusion:

Lab. **CAN NOT** identify RTE and **ONLY** report Squamous epithelium.

American Journal of Kidney Diseases, Vol 46, No 5 (November), 2005: pp 820-829

Urinalysis and Collection, Transportation, and Preservation of Urine Specimens; Approved Guideline—Second Edition

5.3.1 Identifiable Sediment Entities (Formed Elements)

Sediment entities that should be identifiable using a urine microscopic examination include the following:

- Epithelial cells: Transitional (urothelial), Squamous, Renal tubular
- Blood cells: Red blood cells (RBC), White blood cells (WBC)
- Casts: Hyaline, Granular, Waxy, Cellular, RBC, WBC, Bacterial, Broad, Fatty

CLSI 2008

GP16-A2

CLINICAL AND LABORATORY STANDARDS INSTITUTE

(Formerly NCCLS)
Providing NCCLS standards and guidelines, ISO/TC 212 standards, and ISO/TC 76 standards

This document addresses procedures for testing urine, including materials and equipment; macroscopic/physical evaluation; chemical analysis; and microscopic analysis. In addition, a step-by-step outline for collecting, transporting, and storing specimens is included.

A guideline for global application developed through the NCCLS consensus process.

NCCLS

日本　尿沉渣細胞鏡檢標準法的建立
及
對於CKD的篩檢方法

- 1991，尿沉渣檢查法，日本臨床衛生檢查技師會。伊藤機一
- 1995，JCCLS，國內標準法。伊藤機一
- 1995，JCCLS， GP1-P2 尿沉渣檢查法　補遺。伊藤機一， 今井宣子， 八木靖二
- 2000，JCCLS，GP1-P3 。伊藤機一，八木靖二
- 2004，新 Color Atlas 尿檢查。伊藤機一，野崎　司
- 2006，尿沉渣檢查。橫山　貴， 堀田 茂

台灣目前尿液檢驗現況

編號	診療項目	基層院所	地區醫院	區域醫院	醫學中心	支付點數
一、一般尿液檢查(06001-06017) 註：尿常規檢查各項點數累積超過75點者，以75點支付。						
06001C	酸、鹼度反應 PH	v	v	v	v	15
06002C	比重檢查 SP.gr (specific gravity)	v	v	v	v	15
06003C	蛋白質定性檢查 Prorein (qualitative)	v	v	v	v	15
06004C	糖定性檢查Sugar (qualitative) 註：尿糖試紙檢查比照申報	v	v	v	v	15
06005C	尿膽素原檢查 Urobilinogen	v	v	v	v	15
06006C	膽紅素檢查 Bilirubin	v	v	v	v	15
06007C	苯酮體檢查 Ketone body 註：血中丙酮檢查比照申報	v	v	v	v	15
06008C	班尼迪克特反應 Benedict reaction	v	v	v	v	15
06009C	尿沉澄顯微鏡檢查 Sediments 註：包括紅血球、白血球、圓柱體、上皮細胞、粘液、淋巴球、寄生蟲等無染色標本檢查。	v	v	v	v	25
06010C	本周氏蛋白試驗Bence Jones protein	v	v	v	v	25
06011B	乳糜尿之確定Chyuria		v	v	v	40
06012C	尿一般檢查(包括蛋白、糖、尿膽元、膽紅素、尿沈渣、比重、顏色、混濁度、白血球酯酶、潛血、酸鹼度及酮體) General urine examination	v	v	v	v	75
06013C	尿生化檢查(包括蛋白、糖、尿膽元、膽紅素、比重、顏色、混濁度、酸鹼度、白血球酯酶及酮體) Urine biochemistry examination	v	v	v	v	75
06014B	酸、鹼度反應點測PH by PH meter		v	v	v	50
06015C	亞硝酸鹽檢查 Nitrite	v	v	v	v	15
06016B	脂肪染色 Fat stain		v	v	v	25
06017B	白血球酯酶 Leukocyte rsterase		v	v	v	25

第四項生化學檢查 Biochemistry Examination

一、一般生化學檢查 (09001-09136)

編號	診療項目	基層院所	地區醫院	區域醫院	醫學中心	支付點數
09016C	肌酐、尿 Creatinine (U) CRTN	v	v	v	v	40
27065B	微白蛋白 Microalbumin		v	v	v	450
12111C	微白蛋白 (免疫比濁法) Microalbumin (Nephelometry)	v	v	v	v	275

Protein+Sugar+Uro.+Bil+Sediment+S.p.+Color+Turbit+WBC+O.B.+pH+Keto=155點 ≠75點

Protein+Sugar+Uro.+Bil+S.p.+Color+Turbit+pH+WBC+Keto=130點 ≠75點

Leukocyte esterase只存在於Neutrophils

06012C:

Protein+Sugar+Uro.+Bil+Sediment+S.p.+Color+Turbit+WBC+O.B.+pH+Keto =75點

06013C:

Protein+Sugar+Uro.+Bil +S.p.+Color+Turbit+WBC +pH+Keto= 75點

健保嚴重失真給付，導致有無執行Sediment均給付75點
Sediment 需要高度鏡檢能力與人力，給付卻被備註之上限75點限制

依據NFK 2002，ADA 2004之指南，
對於慢性腎病高危險群應施行定期之尿液篩檢
現今，健保局完全沒有訂定高感度之尿液試紙檢驗 (Cre. / Microalbumin) 給付

生化： 09016C Cre.40點 + 12111C Microalbumin 275點= 315點 執行率低

尿液一般檢查: 06012C 75點 執行率高

尿液一般檢查，執行率高，卻對於慢性腎病之早期篩檢率成效不佳。

因為現今尿液檢查的執行重點，尚未達到此項檢驗應有的最佳品質。

尿液檢查的執行重點

~~如何提高品質~~

•檢體的採集

1. 清晨第一次中段尿最佳，可避免姿勢性蛋白尿
2. 隨機之中段尿亦可接受

•程序標準化

1.尿液檢體之收集量 (10,12,15 ml)?

2.尿液化學分析之使用檢體量及剩餘可離心鏡檢之尿量?

3. 離心力與離心時間 (400g, 500g ; 5分)?

3.尿沉渣細胞鏡檢之濃縮檢體倍數 (10:1 , 12:1 ,15:1)?

4 玻片種類與製做方式?

5 .人員鏡檢能力的差異?

•報告標準化

1. Protocol
2. 設定參考值
3. 報告格式與單位
4. 標示出異常報告以供參考

臨床體液鏡檢概述

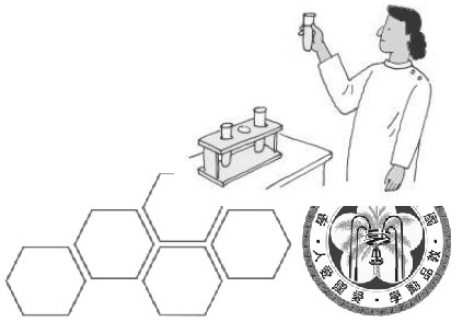
Body fluid之常規檢查項目

◆**Pleural, Pericardial, Ascites**
S.G.
Rivata test
Cell count
WBC Differential count: L:N:M&H
Abnormal cell

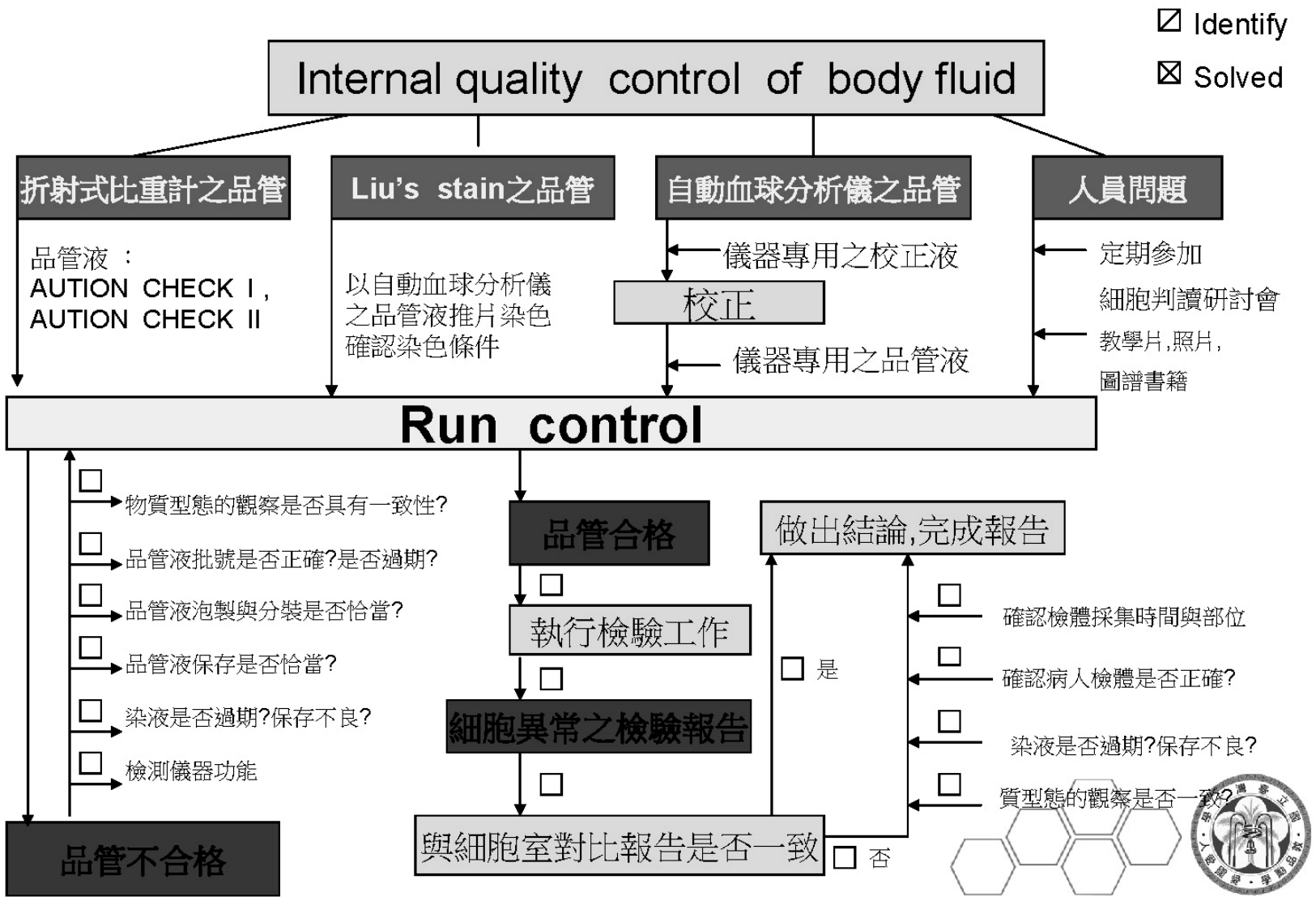
◆**Abnormal cell: Reactive cell, Degenerated cell, Malignant cell**

◆**Synovial Fluid**
Cell count, Crystal

◆**Cerebrospinal Fluid**
RBC count
WBC count
WBC Differential count : L/N
Cryptococcus
Abnormal cell

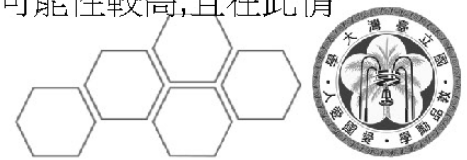


體液檢查品管異常檢查表 __年__月__日，單位____班別____操作者_____主管_____



報告方式

- 體液中RBC的多寡較無臨床意義
- Cell count 的部份:
  建議以"TNC (Total nuclear count)" 來表示，而非"WBC count"
- 細胞分類是指全部有核細胞皆需計數分類
  依淋巴球(L),嗜中性白血球(N) ，中皮細胞(M),組織球或巨噬細胞(H)而分類
- 少數的其它細胞
  ex:漿細胞(plasma cell)可歸入淋巴球計算,
  嗜酸性白血球(Eosinophil)則需另外註明
- 細胞分類之臨床意義:
  1. 病人發燒、胸部X光呈現胸水:
     肺炎合併胸水~~以 PMN 為主
     結核性胸水~~~~以Lymphocyte為主，同時中皮細胞少於1%, 絕少出現5%以上
  2. 病人呼吸困難、胸部X光呈現單側胸水:
     癌症~~~可能出現癌細胞
     結核性胸水~~~~以Lymphocyte為主，同時中皮細胞少於1%, 絕少出現5%以上
- 若只計數 L:N ,而不考慮中皮細胞數,則此分類計數不具任何臨床意義
  1. **L:N:M:H=85：5：1：9**
     結核病可能性高，淋巴瘤、癌症或病毒感染可能性較低
  2. **L:N:M:H=85：5：8：2**
     結核病之可能性極低,因中皮細胞出現5%以上 ，癌症或病毒感染的可能性較高,且在此情形下雖沒有看到惡性細胞,也不能貿然當作結核病治療



退化細胞
Degenerated or Damaged Cells

- 具有濃縮（pyknotic）、濃染細胞核的退化細胞偶而可在體液中被發現。
- 當嗜中性白血球企圖去除外來物質時，可能發生自我消化 （autodigestion）或自我溶解（autolysis）現象，細胞核變的濃縮進而自我分解後，可能出現一個或多個淡紫色的內含物。
- 細胞質顆粒變的較不明顯或發生融合（fuse）。
- 自溶的嗜中性白血球具偏心、濃染、圓形的細胞核和淡色的細胞質，
- 因而相似於有核紅血球，但不同的是，其仍持續帶有細胞質的顆粒。

Synovial Fluid

- MSU (monosodium urate)

  引起痛風（gout）的晶體

  兩端尖細的針狀或桿狀晶體 ， 大小為2～20 μm，0.2~1 μ厚。
  MSU的長軸與補償濾鏡的慢光方向平行時，晶體變黃色
  長軸與補償濾鏡的慢光方向垂直時，晶體變成藍色
  MSU晶體之快光方向平行於晶體的長軸，所以MSU是"負偏光型"
  （negative）

- CPPD (calcium pyrophosphate dihydrate)

  引起"偽痛風"的關節炎以及其他疾病，例如：新陳代謝疾病之甲狀腺功能減退（hypothyroidism）病患的滑膜液中

  兩端方形的短桿狀、菱形、鑽石形或四角形晶體 ，
  大小為2～20 μm， 通常小於10 μ

  CPPD晶體之快光方向垂直於晶體的長軸折光性與MSU相反，為"正偏光型'
  （postive）

Synovial Fluid

- Cholesterol

為細胞外的結晶體，是體液中較大型的結晶體

扁平、似盤狀且缺一角之菱形晶體， 具強雙折光性

關節液中少見，通常與慢性發炎性疾病有關，出現於慢性積水中如類風濕性關節炎

- Hematin (hematoidin)

平行四邊形之晶體

嚴格地說，hematin和hematoidin是不同的物質。

Hematin是一種從血色素分解而來的三價鐵化合物， 並不屬 於結晶體

Hematoidin則是一種在流血或出血約兩週後可出現的結晶體，

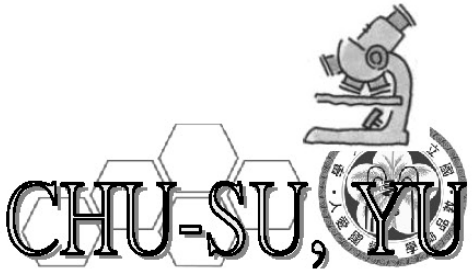
其可存在於細胞內或細胞外。

然而目前仍互用此二名詞。

Cerebrospinal Fluid

- RBC count
- WBC count
- Differential count :

  L/N
- Cryptococcus
- Abnormal cell



計數方式

1．血球計算盤:

WBC：

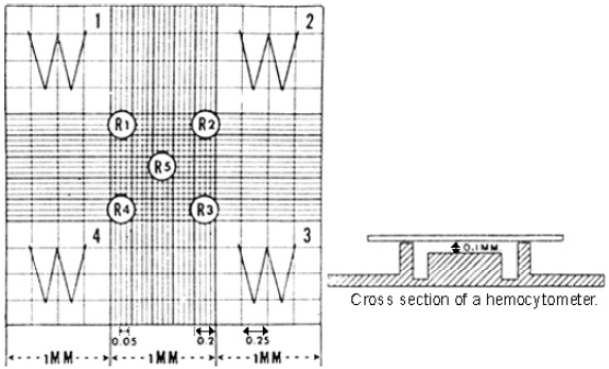
十大方格內之 WBC計數 X 稀釋因子X體積因子= cells / ul

或 九大方格內之 WBC計數 X稀釋因子(10/9) X 體積因子(10/9)=九大方格內之 WBC計數 X 100 / 81

RBC：

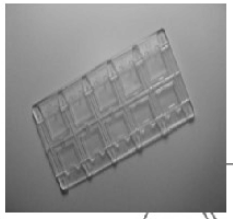
十大方格內之 RBC計數 X 體積因子= cells / ul

或 九大方格內之 RBC計數 X 體積因子(10 / 9)=九大方格內之 RBC計數 X 10/ 9



Cross section of a hemocytometer.

2. S-Y Double Grids Counting Slides 10



C.S.F：

1. Cells少時： 9大格細胞總數 x 1.1 x 稀釋倍數＝ 1 μl細胞數

2. Cells多時： 9小格細胞總數 x 10 x 稀釋倍數＝ 1 μl細胞數

CHU-SU, YU

Thank you for your attention