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# 醫學實驗室Albumin檢驗方法學對臨床判讀之影響

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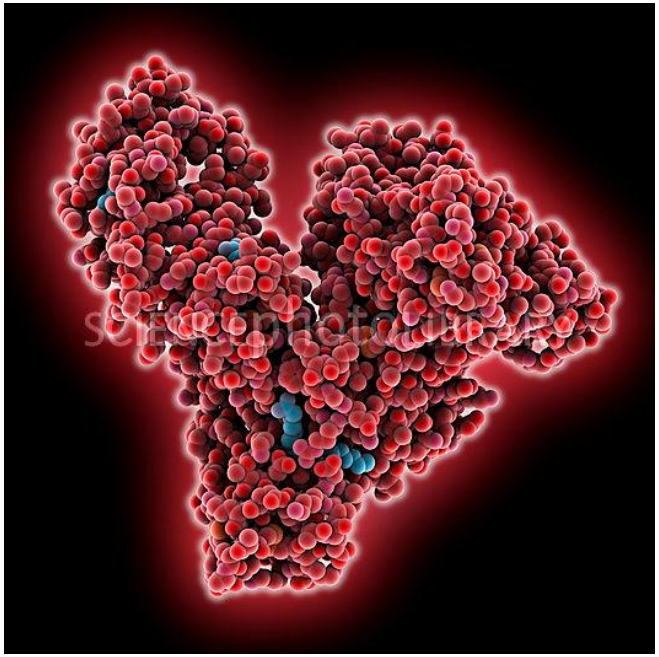
104.12.12

# Agenda

1. Question
2. About Albumin
3. Detection Methods
4. Criteria of ESRD Care
5. ALB-BCG  vs. ALB-BCP
6. Results
7. Conclusions



# Question

血液透析及療養院因Albumin偏低，影響醫療照護品質的解讀。

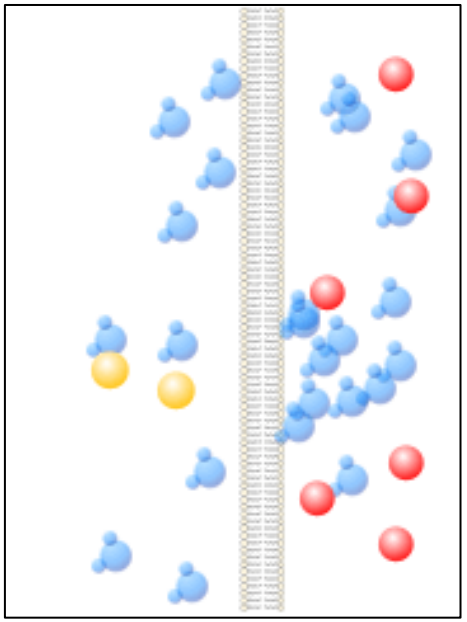
# About Albumin

Protein-energy nutritional status. Albumin is a powerful predictor of mortality and morbidity.

慢性腎臟病患者常見「蛋白質-熱量營養不良」，與患者預後有關。Albumin被視為營養是否足夠的指標。


# About Albumin

1. Concertration in blood: 3.5-5.2 (g/dL)
2. Half-Life: 15-19 days
3. pI: 4-5.8
4. 585 amino acids
5. MW: 66438 Da
6. Function: Maintain oncotic pressure, Transports fatty acid, bilirubin, and other organic molecules; bind calcium, drugs.

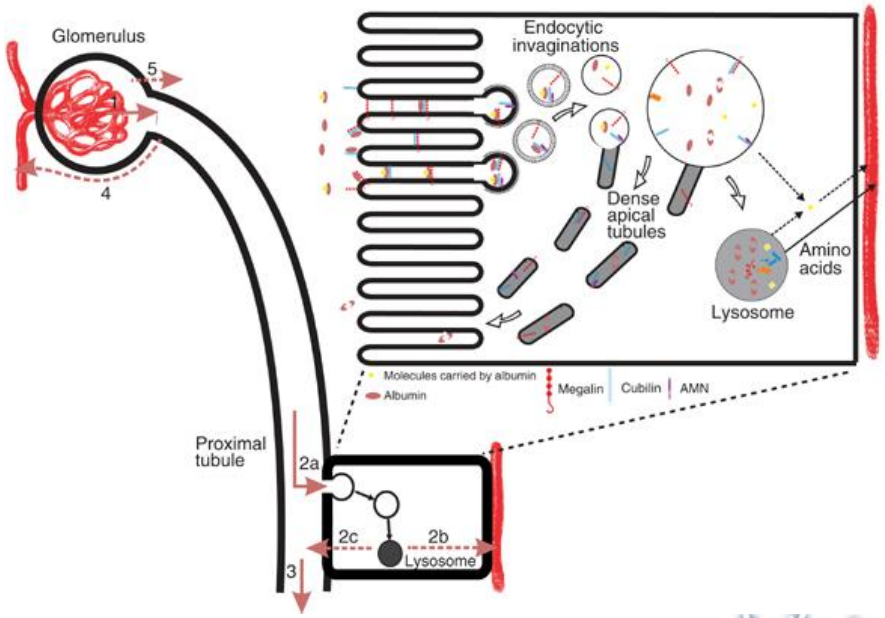


http://www.blobs.org/mobile/article.php?article=65&question=4#article.php?article=67&question=1

Tietz Textbook of Clinical Chemistry and Molecular Diagnostics 5'th edition

# About Albumin

7. Synthesis: Hepatocytes
8. Catabolism: Pinocytosis by multiple tissues, with lysosomal degradation of protein to amino acids.




Renal albumin absorption in physiology and pathologyH Birn and E I Christensen

# About Albumin

9. Clinical Significance of Decreased Albumin

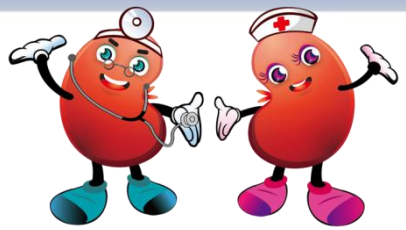
(1) Analbuminemia
(2) Inflammation
(3) Malnutrition
(4) Hepatic Disease
(5) Edema and Ascites
(6) Urinary/GI Loss
(7) Kidney Disease
(8) Protein-Calorie
(9) Burn Injury

(Normally, only 10-20% of Total catabolized)

# Detection Methods

Albumin是具有與許多陰離子有機物，如脂肪酸、膽紅素、激素、藥物，甚至於色素或指示劑結合的特性。故設計出最為被廣泛使用即BCG (bromosresol green)及BCP (bromocresol purple)方法，使Albumin與色素結合，導致顏色改變，進而進行偵測。

# Criteria of ESRD Care



隨台灣公共衛生進步及人民壽命延長，台灣地區接受透析治療患者人數逐年提高，導致醫療支出大幅增加。藉由國健局、衛生署、台灣腎臟學會進行HOPE軟體開發計畫，共同統計自健保啟用(民國84年)至民國90年共34881位末期腎衰竭(ESRD, End Stage Renal Disease)患者之各項生化資料，並開始執行全民健康保險慢性腎衰竭病人門診透析服務品質提升獎勵計畫。

# 血液/腹膜透析病人常用檢查

| | | | | | |
|---|---|---|---|---|---|
| 洗前洗後 BUN | **Albumin** | Fe | Kt/V | HBsAg | Weekly Kt/V |
| 洗前洗後 Cre | Globulin | TIBC | URR | HBeAg | Weekly Clcr |
| Na | GOT | Ferritin | | Anti-HBs | Peritoneal Clcr |
| K | GPT | WBC | | Anti-HBc | Urine Clcr |
| Ca | Cholesterol | Hb | | Anti-HCV | PET |
| IP | TG | Hct | | STS-RPR | nPNA |
| Alk-p | UA | MCV | | TPHA | Weekly Kt/V |
| Glucose | HbA1C | PLT | | HIV Ab | Weekly Clcr |

臨床檢驗數據判讀-腎臟-徐邦治醫師

# Criteria of ESRD Care

1. 民國84~90年度ESRD統計結果

| | BCG-ALB | BCP-ALB |
|---|---|---|
| 血液透析Hemodialysis | 3.8±0.4 | 3.6±0.5 |
| 腹膜透析Peritoneal dialysis | 3.6±0.5 | 3.2±0.5 |

2. 由統計結果訂定照護指標：

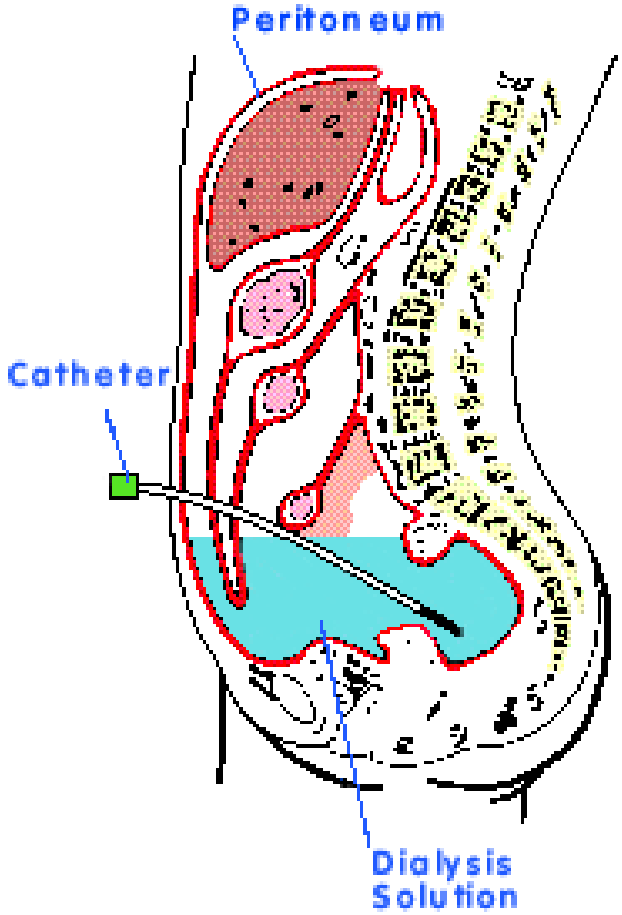
Albumin ≧3.5 g/dL (BCG)或 3.0g/dL (BCP)，合格率≧75%

# Hypoalbuminemia低蛋白血症
## --腹膜透析(Peritoneal dialysis)常見原因

1. 透析過程蛋白質流失：人體腹膜膜孔比血液透析人工腎臟膜孔大，中大分子易流失
2. 飲食蛋白質攝取不足： Anorexia、 Abdominal Distension、 Peritonitis、 Fullness、 Unpalatable or inadequate diets
3. Metabolic acidosis：導致噁心、嘔吐、胃口差、影響內分泌、骨代謝、營養狀態等...
4. 透析不足(Underdialysis)

http://blog.tmu.edu.tw/d301090006/PD%202010.pdf

# Hypoalbuminemia低蛋白血症
## --腹膜透析(Peritoneal dialysis)常見原因



# Criteria of ESRD Care

最新104年度全民健康保險慢性腎衰竭病人門診透析服務品質提升獎勵計畫，血液/腹膜透析照護指標項目及評分標準，血清白蛋白(Albumin ≧3.5 g/dL (BCG)或 3.0g/dL (BCP)，受檢率≧95%且合格率≧70%。

# ALB-BCG vs. ALB-BCP

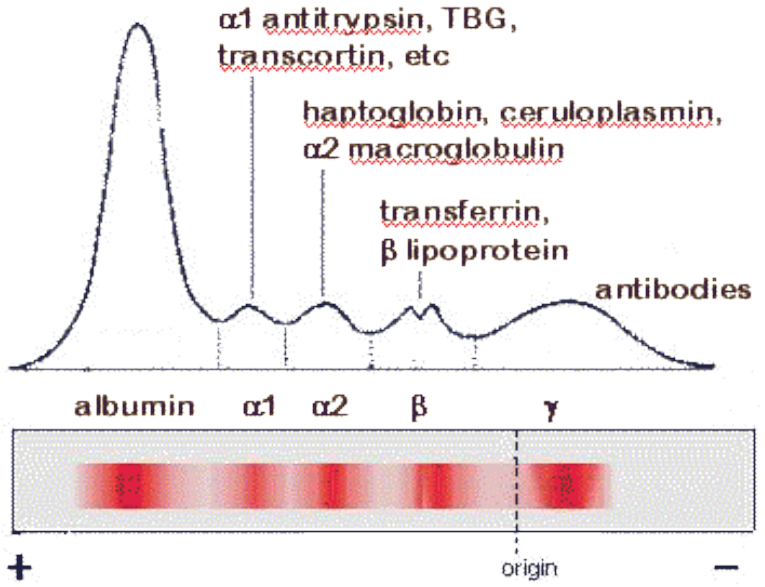
1. ALB-BCG因α1 (含α1-antitrypsin, α1- fetoprotein等)與 α2(含α 2-macroglobulin, haptoglobin等) globulin干擾而增加。
2. Globulin:

α1: 100-400(mg/dL),2.5-5%

α2: 400-1200(mg/dL),7-13%

β: 500-1100(mg/dL),8-14%

γ: 500-1600(mg/dL),12-22%




http://pro2services.com/lectures/Winter/Proteins/protein.htm

# ALB-BCG vs. ALB-BCP

3. Positive Acute Phase Response (APR)

   α1-antitrypsin, C-reactive protein, Ceruloplasmin, Fibrinogen, Haptoglobin, Procalcitonin, C3, C4…

4. Negative Acute Phase Response (APR)

   Albumin, IGF-1, Prealbumin, Transferrin…

# ALB-BCG vs. ALB-BCP

5. The bromocresol green assay, but not the modified bromocresol purple assay, overestimates the serum albumin concentration in nephrotic syndrome through reaction with α2-macroglobulin.

Ann Clin Biochem. 2015 Feb 11. pii: 0004563215574350

# ALB-BCG vs. ALB-BCP

6. Albumin concentration determined by the modified bromocresol purple method is superior to that by thebromocresol green method for assessing nutritional status in malnourished patients with inflammation.

Ann Clin Biochem. 2013 Nov;50(Pt 6):576-84. doi: 10.1177

# ALB-BCG vs. ALB-BCP

7. ALB-BCP 雖不受Globulin干擾，但會因血液透析病患體內CMPF (3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid, is a metabolite produced endogenously from dietary sources of furan fatty acids. The richest source of furan fatty acids in human diet is fish.) 干擾BCP與albumin的結合而降低。因此洗腎的腎臟病患比非洗腎的腎臟病患ALB-BCP低0.3 g/dL。

# ALB-BCG vs. ALB-BCP

8. The degree of underestimation appeared to be well correlated to the serum concentration of 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF), a major endogenous ligand substance present in uremia serum. CMPF inhibited in vitro the binding of BCP to serum protein and human serum albumin. Our results suggest that CMPF is a major interfèrent in the underestimation of the serum albumin concentration by the BCP method in uremia.

Clin Chim Acta. 1987 Jul 30;167(1):89-96.

# ALB-BCG vs. ALB-BCP

9. The accumulation of CMPF in the sera of patients with chronic renal failure may reflect the 'chronicity‘ of renal failure. Plasma exchange was more effective than direct hemoperfusion for the elimination of CMPF retained in uremic serum.

Nephron. 1988;49(4):277-80.

# ALB-BCG vs. ALB-BCP

10. CMPF was recently shown to be elevated in fasting plasma in individuals with gestational diabetes and type 2 diabetes, and mechanistically high level of CMPF was linked to β cell dysfunction.

PLoS One. 2015 Apr 15;10(4):e0124379. doi: 10.1371

# ALB-BCG V.S. ALB-BCP

11. Unselect Patients

ALB-BCG (g/dL) = 0.55 + ALB-BCP (g/dL)

Nephrol Dial Transplant (2001) 16:1925-1929

**Table 1.** Serum albumin by methodology and clinical group

| | *n* | Serum albumin g/l | | |
|---|---|---|---|---|
| | | $Alb_{BCG}$ (mean ± SD) | $Alb_{BCP}$ (mean ± SD) | $Alb_{BCG}$–$Alb_{BCP}$ (mean ± SD) |
| Unselected in-patients | 222 | 33 ± 5.5 | 28 ± 6.0 | 5.3 ± 1.5 |
| Unselected out-patients | 158 | 41 ± 4.7 | 36 ± 5.0 | 5.2 ± 1.3 |
| Haemodialysis patients | 77 | 38 ± 3.1 | 33 ± 3.6 | 5.2 ± 1.3 |
| Peritoneal dialysis patients | 13 | 31 ± 5.2 | 26 ± 5.5 | 5.5 ± 1.1 |
| Renal transplant patients | 35 | 39 ± 3.6 | 34 ± 3.8 | 5.5 ± 1.2 |
| Renal clinic patients | 30 | 29 ± 6 | 24 ± 6.6 | 5.5 ± 1.2 |
| Overall | 535 | 36 ± 6.1 | 31 ± 6.5 | 5.5 ± 1.4 |

# ALB-BCG V.S. ALB-BCP

12. BCP 與 BCG的國內外使用機構比率

| | BCG機構數 | BCP機構數 | 比率(%) |
|---|---|---|---|
| CAP | 2782 | 2272 | 55/45 |
| 台灣醫檢學會 | 527 | 46 | 92/8 |

資料來源：CAP,2015,C-A;台灣醫檢學會2015第一次

# Conclusions

1. 由於ALB使用不同方法學造成數值的差異而影響GLO及A/G ratio計算，可能進而影響醫師的判讀。
2. 二種方法學在 ALB < 3.5 g/dL 與> 3.5 g/dL上下的相關係數有顯著差異。因此以其中一方法學檢測，再以單一係數公式進行換算，所得到的換算數值與實際測量值可能會有偏差。

# Conclusions

3. 除了方法學的不同可能造成數值的差異以外，病患體內其他內源性的物質也可能是影響檢驗數值差異的原因。
4. 臨床端不清楚實驗室使用的偵測方法學可能導致數據判讀錯誤，影響臨床照護成效。

# Reference

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# Thank You