Kidney Function Tests (KFTs)

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Composition and Properties of Urine

- Appearance
  - almost colorless to deep amber; yellow color due to urochrome, from breakdown of hemoglobin (RBC's)
- Odor - as it stands bacteria degrade urea to ammonia
- Specific gravity
  - density of urine ranges from 1.000 -1.035
- Osmolarity : Half the osmolality of normal urine is due to urea, and the other Half is mainly due to NaCl.
  - (blood - 300 mOsm/L) ranges from 50 mOsm/L to 1,400 mOsm/L in dehydrated person
- pH - range: 4.5 - 8.2, usually 6.0
- Chemical composition: 95% water, 5% solutes
  - urea, NaCl, KCl, creatinine, uric acid

Renal Function Tests

- Salt Balance
  - Tests: Na+, Cl-, K+ Aldosterone, Renin
- Acid Base Balance Tests
  - pH, HCO3, NH4, Acid loading, Urinary Anion Gap
- Water Balance Tests
  - specific gravity, osmolarity, water deprivation testing, ADH
- Nutrients Retention Tests
  - proteins, sugar, amino acids, phosphate
- Waste Products Secretion Tests
  - Tests: urate, oxalate, bile salts

Renal Function Tests 2

- Endocrine Function Tests
  - Target organ
    - ADH (water balance)
    - Aldosterone (salt balance)
    - Parathyroid hormone (Ca++, Mg++)
  - Production
    - Erythropoietin
    - 1, 25 dihydroxycholecalciferol
- Kidney Disease Prediction Tests
  - eGFR
  - Urine Albumin
  - Albumin Creatinine Ratio (ACR), (UACR)
  - Renal Clearance Tests

Chronic Kidney Disease (CKD) Markers

- **Urine Albumin**
  - U-Alb (mg/24h)
  - UACR (mg/g) = Albumin Creatinine Ratio

$$\frac{\text{Urine albumin (mg/dL)}}{\text{Urine creatinine (g/dL)}} = \text{UACR in mg/g} \approx \text{Albumin excretion in mg/day}$$

  - Superior Method to predict KD in Diabetes

Definitions

1. High Albuminuria:
   - 30-300 mg/24h
   - 30-300 mg/g
2. Very High Albuminuria (Overt Nephropathy)
   - >300 mg/24h
   - >300 mg/g

NKDEP National Kidney Disease Education Program

American Diabetes Association.

Chronic Kidney Disease (CKD) Markers

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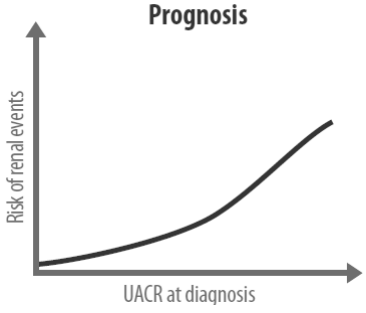
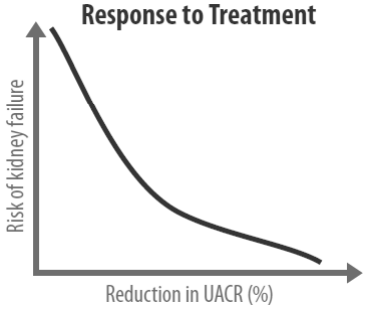
At least 2+ of 3 repeats is diagnostic (3-6 m intervals)

- Start annual testing in DM and/or KD
  - Type 1: at puberty or 5 y after diagnosis
  - Type 2: at the time of diagnosis





Renal Function Tests 3

- Tests of Glomerular Filtration Rate (GFR)
  Urea, Creatinine, **Creatinine Clearance,** Cystatin C, **eGFR**
  GFR= NFP × Kf ≈ 125 ml/min

Renal Clearance of Therapeutics:

- A hypothetical calculation of plasma volume of unmetabolized drug cleared through the kidneys in unit time.
- A measurement of the Renal Excretion Ability
- Factors influencing RC:
  - Renal blood flow (Filtration)
  - Urinary pH
  - Tubular Reabsorption
  - Tubular Secretion

  } Excretion= Filtration – Reasoption + Secretion

Renal Function Tests 3

Excretion= Filtration – Reabsoption + Secretion

(1) $$V\frac{dC}{dt} = -K \cdot C + m$$

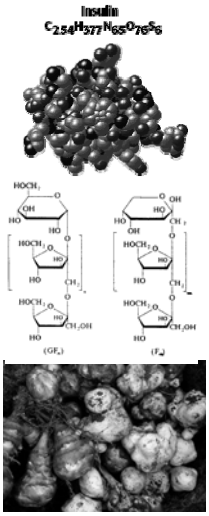
(11) $$K = \frac{C_U \cdot Q}{C_B}$$

C_U = urine concentration [mg/mL]
Q = urine flow (volume/time) [mL/min] (often [mL/24 hours])
C_B = plasma concentration [mg/mL])

1926: Poul Brandt Rehberg (1989-1989)

Normal Clearance Values (ml/min)		
Glucose	0	completely reabsorbed
Inulin	125	not reabsorbed & not secreted
PAH	625	completely secreted

Inulin Clearance



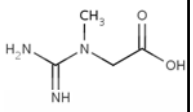
Inulin is the ideal indicator for determination of GFR, because:

1. It is a polyfructose (from Artichokes) without effect on GFR.
2. It has a spherical configuration and a molecular weight of 5000.
3. It is an exogenous substance - not synthesised or broken down in the body.
4. It filters *freely* through the glomerular barrier. Inulin is uncharged and not bound to proteins in plasma. It crosses freely most capillaries and yet does not traverse the cell membrane (distribution volume is ECV). Since one litre of plasma contains around 0.94 l of water, the ultrafiltrate concentration of inulin is $C_p/0.94$.
5. All ultrafiltered inulin molecules pass to the urine. In other words, they are neither reabsorbed nor secreted in the tubules.
6. Inulin is non-toxic and easy to measure.
7. Sinistrin is often preferred to the alternative, inulin, because it is highly soluble in water and easier to handle. For the application as a renal diagnostic an aqueous solution of Sinistrin is approved under the trade name: Inutest.

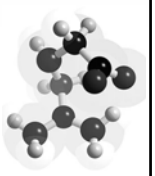
- Inulin must be infused intravenously, and the method is not necessary in clinical routine.
- The normal values for both sexes decrease with age to *70 ml* per min after the age of *70*.

Creatinine Clearance

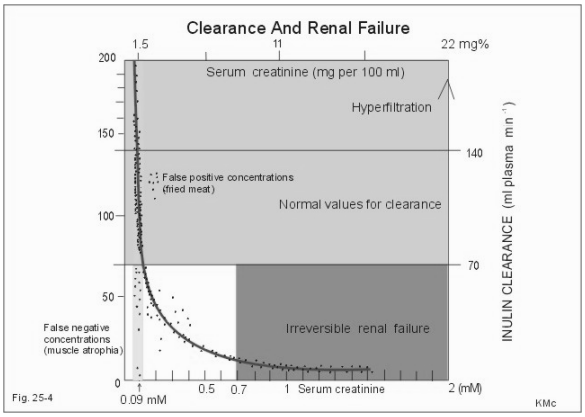
C4 H9 N3 O2



- In a 70-kg person creatinine is produced at a constant rate of *1.2 mg per min* (1730 mg daily).
- Both the serum creatinine and the renal creatinine excretion fluctuate throughout the day. Therefore, it is necessary to collect the urine for 6-24 hours
- Theoretically, two small errors disturb the picture, but both are overestimates.
- At the normally low plasma concentrations of creatinine, a modest tubular secretion of creatinine from the blood is detectable resulting in up to 15% overestimation of the creatinine excretion flux. Most laboratories measure creatinine in *serum* instead of plasma, which results in an overestimation of plasma creatinine.
- Thus, calculation of a fraction with both an overestimated nominator and denominator results in a value close to that of GFR in almost all situations, where the renal function is near normal.
- With progressive renal failure the plasma creatinine rises, and the creatinine secretion increases the nominator in the clearance expression even more, so the measured clearance will overestimate GFR. Still, the clearance provides a fair clinical estimate of the renal filtration capacity (GFR).



Creatinine Clearance vs Serum Creatinine

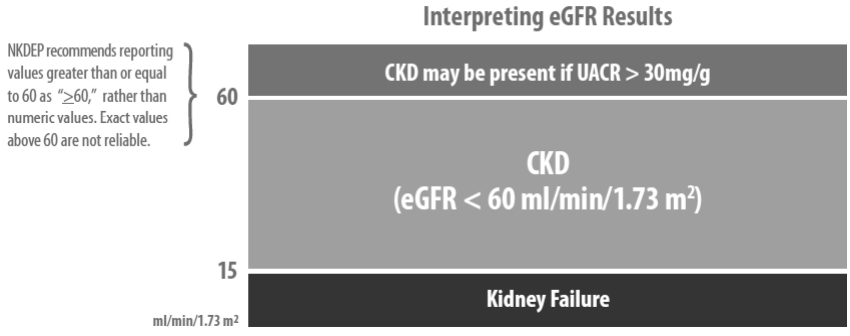


In most cases a normal creatinine clearance (above 70 ml plasma per min at any age) is comparable with the normal range for serum.

The serum creatinine concentration is inversely proportional to the creatinine clearance, and also a good estimate of GFR. Renal failure is almost always *irreversible*, when the serum creatinine is above 0.7 mM.

eGFR

- eGFR is more accurate than serum creatinine alone. Serum creatinine is affected by muscle mass, and related factors of age, sex, and race.
- eGFR is not reliable for patients with rapidly changing creatinine levels, extremes in muscle mass and body size, or altered diet patterns.



Cockcroft-Gault Formula for Estimation of GFR

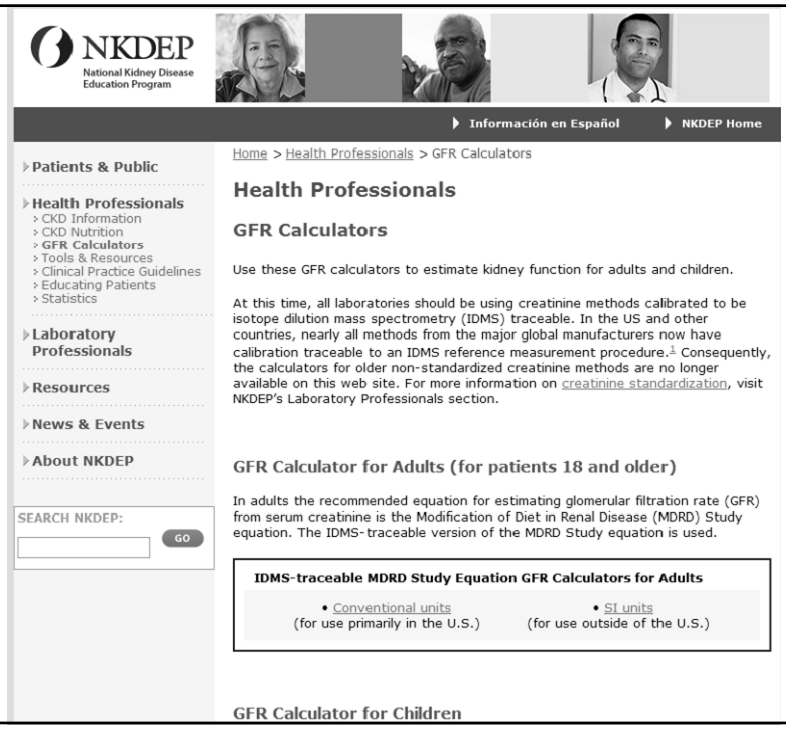
Cockcroft-Gault Formula:

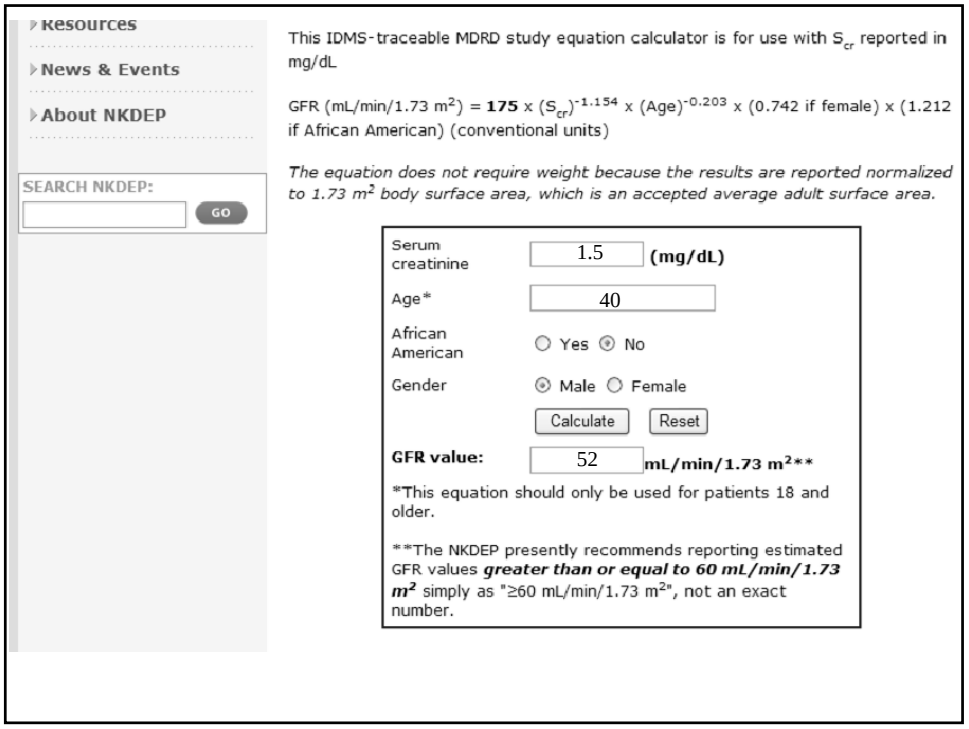
$$\text{GFR} = \frac{K \times (140 - \text{age}) \times \text{Body weight}}{\text{Serum creatinine } (\mu\text{mol/L})}$$

where K is a constant that varies with sex:
1.23 for male & 1.04 for females.

The constant K is used as females have a relatively lower muscle mass.

This formula overestimates the GFR if the patient is obese.

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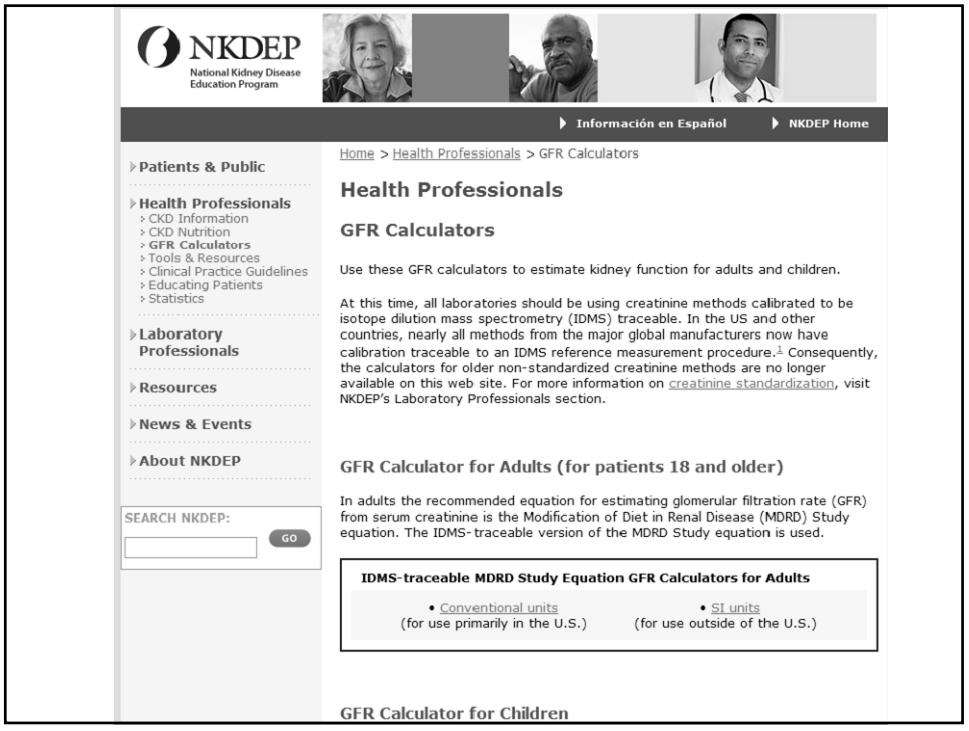
This IDMS-traceable MDRD study equation calculator is for use with S_{cr} reported in mg/dL
GFR (mL/min/1.73 m^2) = **175** x $(S_{cr})^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.212 if African American) (conventional units)
The equation does not require weight because the results are reported normalized to 1.73 m^2 body surface area, which is an accepted average adult surface area.
Serum creatinine
1.5
(mg/dL)
Age*
40
African American
Yes
No
Gender
Male
Female
Calculate
Reset
GFR value:
52
mL/min/1.73 m^2**
*This equation should only be used for patients 18 and older.
The NKDEP presently recommends reporting estimated GFR values ***greater than or equal to 60 mL/min/1.73 m^2* simply as "≥60 mL/min/1.73 m^2", not an exact number.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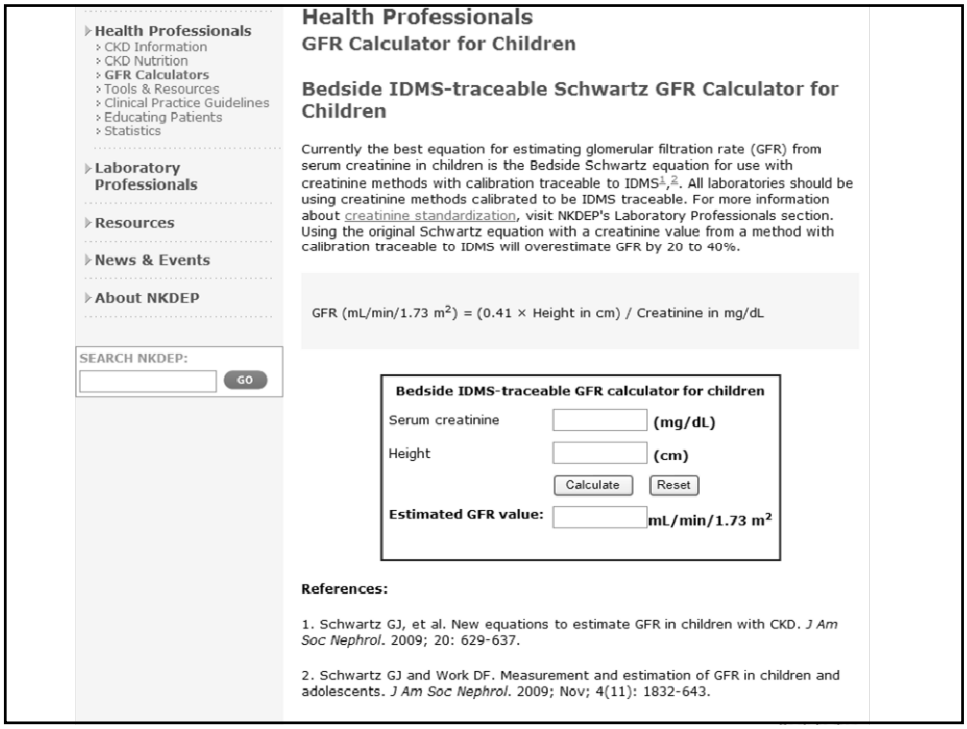
GFR Calculators
Use these GFR calculators to estimate kidney function for adults and children.
At this time, all laboratories should be using creatinine methods calibrated to be isotope dilution mass spectrometry (IDMS) traceable. In the US and other countries, nearly all methods from the major global manufacturers now have calibration traceable to an IDMS reference measurement procedure.[1] Consequently, the calculators for older non-standardized creatinine methods are no longer available on this web site. For more information on creatinine standardization, visit NKDEP's Laboratory Professionals section.
GFR Calculator for Adults (for patients 18 and older)
In adults the recommended equation for estimating glomerular filtration rate (GFR) from serum creatinine is the Modification of Diet in Renal Disease (MDRD) Study equation. The IDMS-traceable version of the MDRD Study equation is used.
IDMS-traceable MDRD Study Equation GFR Calculators for Adults
• Conventional units (for use primarily in the U.S.)
• SI units (for use outside of the U.S.)
GFR Calculator for Children



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GFR Calculator for Children

Bedside IDMS-traceable Schwartz GFR Calculator for Children

Currently the best equation for estimating glomerular filtration rate (GFR) from serum creatinine in children is the Bedside Schwartz equation for use with creatinine methods with calibration traceable to IDMS[1,2]. All laboratories should be using creatinine methods calibrated to be IDMS traceable. For more information about creatinine standardization, visit NKDEP's Laboratory Professionals section. Using the original Schwartz equation with a creatinine value from a method with calibration traceable to IDMS will overestimate GFR by 20 to 40%.

GFR (mL/min/1.73 m^2) = (0.41 × Height in cm) / Creatinine in mg/dL

Bedside IDMS-traceable GFR calculator for children

Serum creatinine ____ (mg/dL)

Height ____ (cm)

Calculate Reset

Estimated GFR value: ____ mL/min/1.73 m^2

References:

1. Schwartz GJ, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol*. 2009; 20: 629-637.

2. Schwartz GJ and Work DF. Measurement and estimation of GFR in children and adolescents. *J Am Soc Nephrol*. 2009; Nov; 4(11): 1832-643.

Creatinine Standardization

- Based on Isotope dilution /mass spectrometry measurements of creatinine standards
- Permits estimation and correction of creatinine and eGFR bias at the laboratory level.
- Importance of Standardization
  - Low bias creatinine:
    - Causes inappropriately increased eGFR
    - Patients will not receive the benefits of more intensive investigation of treatment.
  - High bias creatinine:
    - Causes inappropriately decreased eGFR
    - Patients receive investigations and treatment which is not required. Wastes time, resources and increases anxiety.

Thank you for your Attention!
Questions?