Pseudohyperkalemia: causes, investigations, and prevention

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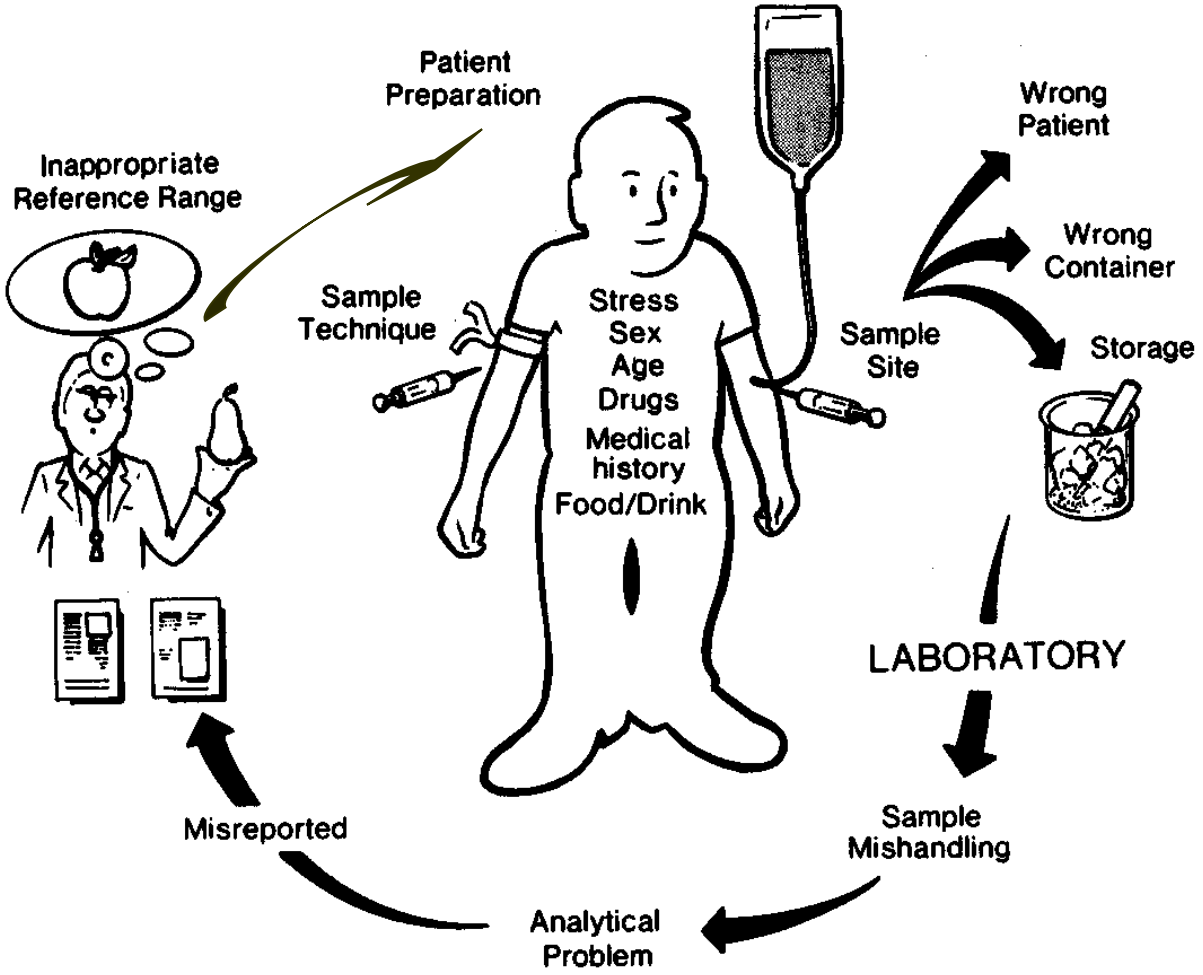
Objectives:

- To recognize the common causes of pseudohyperkalemia
- To understand the causes of uncommon fictitious and reverse pseudohyperkelemia
- To interpret, investigate, and prevent pseudohyperkalemia

Complete Cycle for Lab Testing



Cases

KCL MIX-UP LEADS TO DEATH

In 2002, an 83 year old woman was admitted to a hospital with a broken hip and was receiving parenteral nutrition via a PICC line. The nurse mistakenly used an extra vial of KCL as saline solution in her pocket to flush the patient's PICC line.

In 2004, two critically ill patients died after being mistakenly given potassium chloride solution (KCL) while being treated for dialysis.

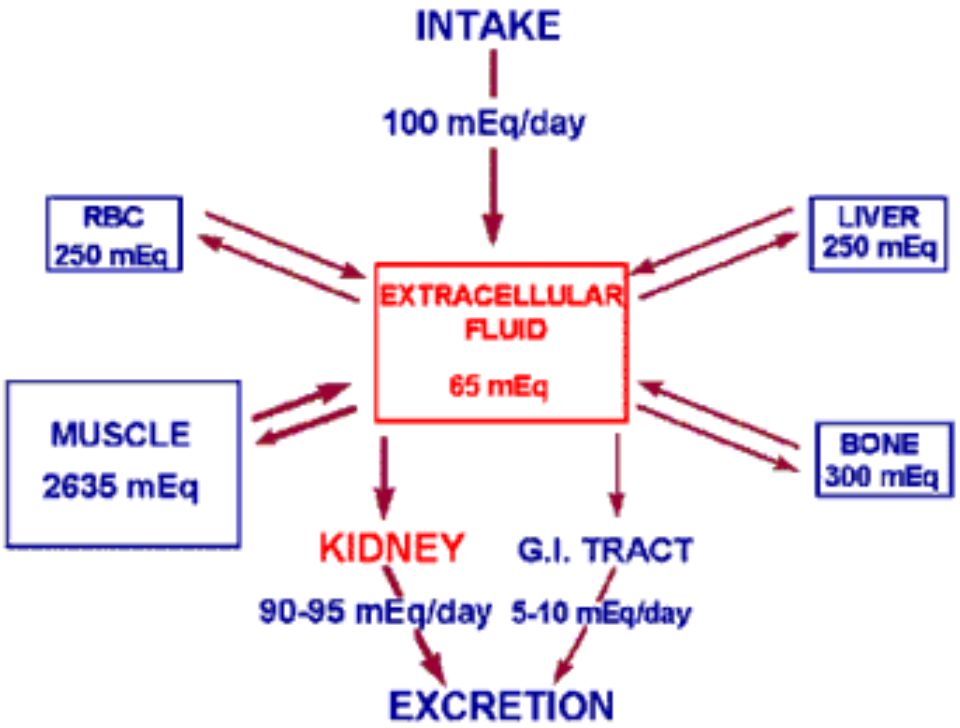
An investigation on the death of a 74-yr-old man

The patient's initial potassium was 8.9 mmol/L on blood gas. The specimen was not hemolyzed but was very lipemic. The tech called the ER to find out if specimen could be contaminated with TPN or drawn in line. The nurse indicated that there was no TPN given but the patient had many lines running. Specimen was recollected and the potassium 8.6 mmol/L. Subsequent measurements from this patients were 7.8 and 7.6 mmol/L.

Results were cancelled due to contamination:

Lessons: 1).Simply thought contamination, 2). Did not follow investigation protocol and critical value reporting, 3). Lipemia cause pseudohypokalemia not hyperkalemia and no interference on direct ISE.

NORMAL POTASSIUM DISTRIBUTION AND BALANCE



- Over 90% of body potassium is contained within cells, principally muscle cells, and is readily exchangeable. Only 2.5% is in ECF.
- Daily intake approximately equals amount in ECF.
- The kidney excretes 90-95% of the daily intake. The rest is excreted by the GI tract.

Facts:

In tissue cells, average potassium concentration is 150 mmol/L.

In RBC, the concentration is 105 mmol/L (about 25 times its plasma concentration)

WBC: 120 mmol/L

Platelets: 100 mmol/L

High intracellular potassium concentration is maintained by Na^+, K^+-ATPase with slowly diffused outward via cell membrane.

Causes of Hyperkalemia:

➢ Ineffective elimination:

- Renal insufficiency
- Medication that interferes with urinary excretion: ACE inhibitors and angiotensin receptor blockers, potassium-sparing diuretics (amiloride and spironolactone), penicillin, cyclosporin A, tacrolimus.
- Mineralocorticoid deficiency or resistance: Addison's disease, Aldosterone deficiency, some forms of congenital adrenal hyperplasia, Type IV renal tubular acidosis (resistance to aldosterone)
- Gordon's syndrome: a type of pseudohypoaldosteronism with hypertension and hyperkalemia.

➢ Excessive release from cells

- Rhabdomyolysis, burns, or any cause of rapid tissue necrosis, including tumor lysis syndrome, massive blood transfusion or hemolysis.
- Shifts out of cells caused by acidosis, low insulin levels, beta-blocker therapy, digoxin overdose or the paralyzing agent succinylchlorine, Epsilon-aminocaproic acid, hyperglycemia.

Causes of Hyperkalemia (cont'd):

➢ Excessive intake

Excess intake with salt-substitute, potassium-containing dietary supplements, or potassium chloride (KCl) infusion. Hyperkalemia by potassium intake would be seen only with large infusions of KCl or oral doses of several hundred milliequivalents of KCl.

➢ Lethal injection

Hyperkalemia is intentionally brought about in an execution by lethal injection.

Heparin-induced hyperkalemia in chronic hemodialysis patients

- 2 patients received cross over UH and LMWH dialysis (each for 1 week), the plasma K^+ level was higher with UH than with LMWH.
- This property makes LMWH use preferable to that of UH (inhibits aldosterone) in patients with elevated predialysis kalemia.

TABLE 1. *Comparison of unfractionated heparin (UH) and low molecular weight heparin (LMWH) protocols*

	UH IU	LMWH aXa U	
Plasma potassium (m*M*)	5.66 ± 0.83	5.15 ± 0.68	$p < 0.05$

Hottelart C et al. Artif Organs. 1998;22(7):614-7.

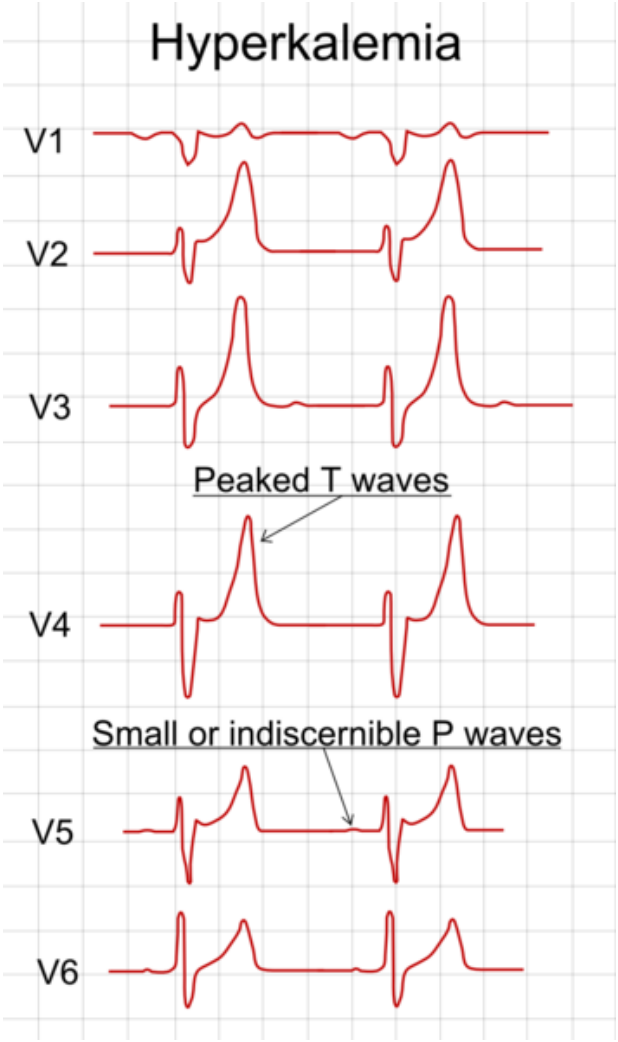
Hyperkalemia

- **Hyperkalemia is defined as a potassium level greater than 5 mmol/L**
- **Ranges are as follows**
  - **Mild**

    5-6.0 mmol/L (>5.3 or 5.5mmol/L elevated)
  - **Moderate (Emergency)**

    6.1-7.0 mmol/L
  - **Severe (Life threatening)**

    7.0 mmol/L and greater



We're a little concerned
about your potassium levels.

Pseudohyperkalemia

- The phenomenon of pseudohyperkalemia was first reported by Hartmann and Mellinkoff in 1955 (Hartmann RC, Mellinkoff SM. J Clin Invest 1955;34:938.).

- Pseudohypekalemia is characterized by marked elevation of serum potassium levels (>0.4 mmol/L) as compared to the normal plasma potassium concentration in the absence of clinical evidence of electrolyte imbalance

- Due to the release of potassium from cells and platelets during the processes of specimen collection and clot formation.

Factors Resulting in Spurious Potassium Levels

(1) Leaving Tourniquet on for Extended Time

(2) Excessive Fist Clenching

(3) Arm in Upward Position

(4) Betadine (potassium iodine)

(5) Inappropriate Order of Draw

(6) Drawing Above IV Site

(7) Benzalkonium Heparin for Coating Catheters (ISE interference)

(8) Vigorously Mixing Tubes

(9) Collection Technique (traumatic venipuncture and small-gauge needle)

(10) Chilling Blood

(11) Re-centrifugation

(12) Pneumatic Tube Systems

(13) Delayed separation of blood cells from serum/plasma

(13) Thrombocytosis and Myeloproliferative Disorders

(14) Dehydration

(15) Familial Pseudohyperkalemia

Collection techniques: Fist Clenching

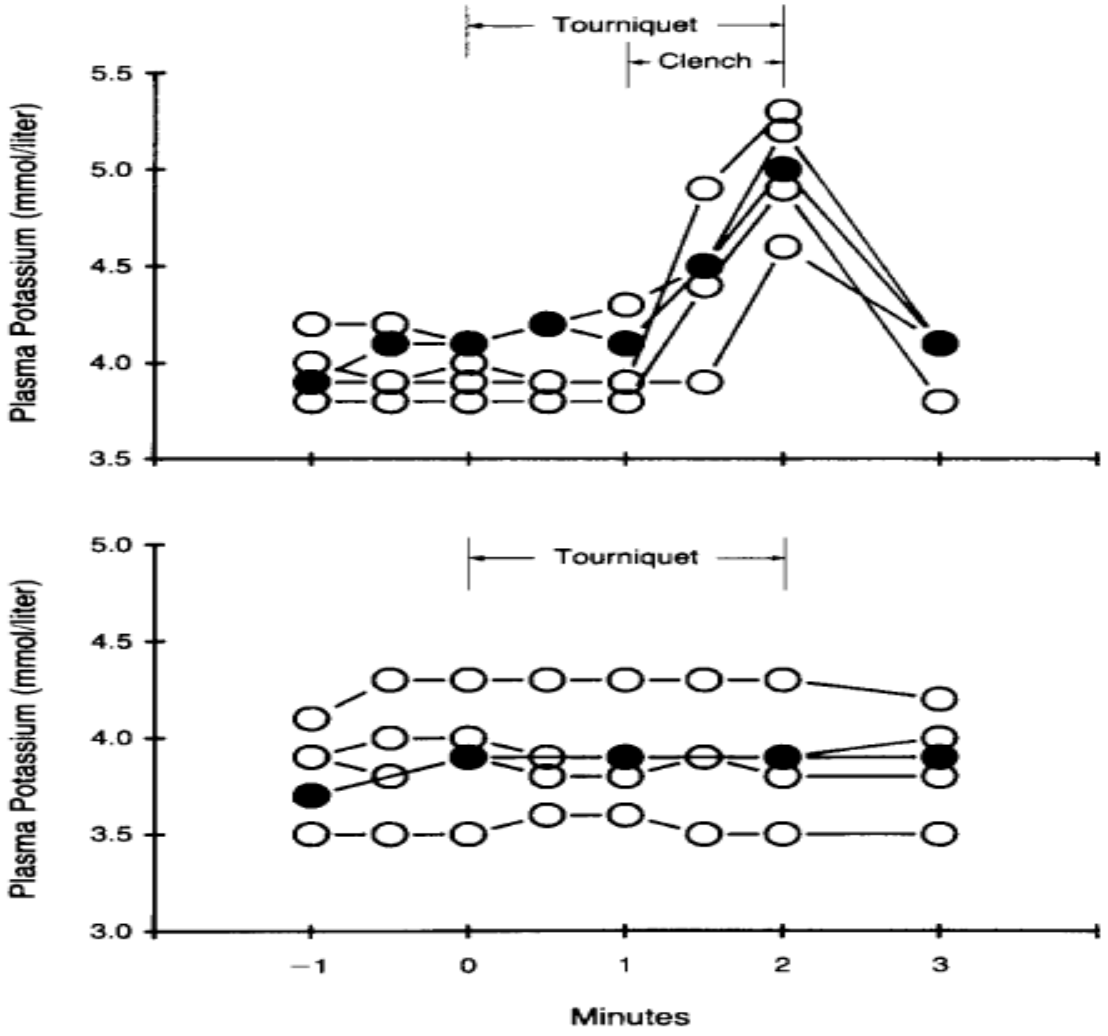


Figure 1. Effects of the Application of a Tourniquet plus Fist Clenching (Upper Panel) and Tourniquet Alone (Lower Panel) on Plasma Potassium Concentrations.

Don BR et al. N Engl J Med. 1990;322:1290-2.

Fist Clenching During Phlebotomy

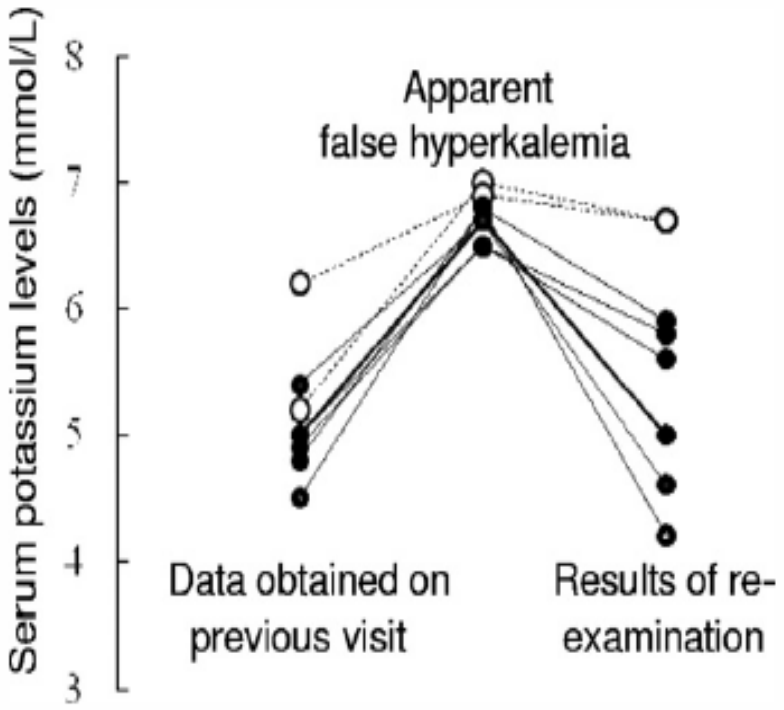


Figure 1. Pseudohyperkalemia observed in 6 samples obtained without using standard precautions. As a result of repeated examination with application of a tourniquet alone, 6 cases (closed circles) were confirmed as pseudohyperkalemia. Two other cases (open circles) eventually were diagnosed as chronic renal failure.

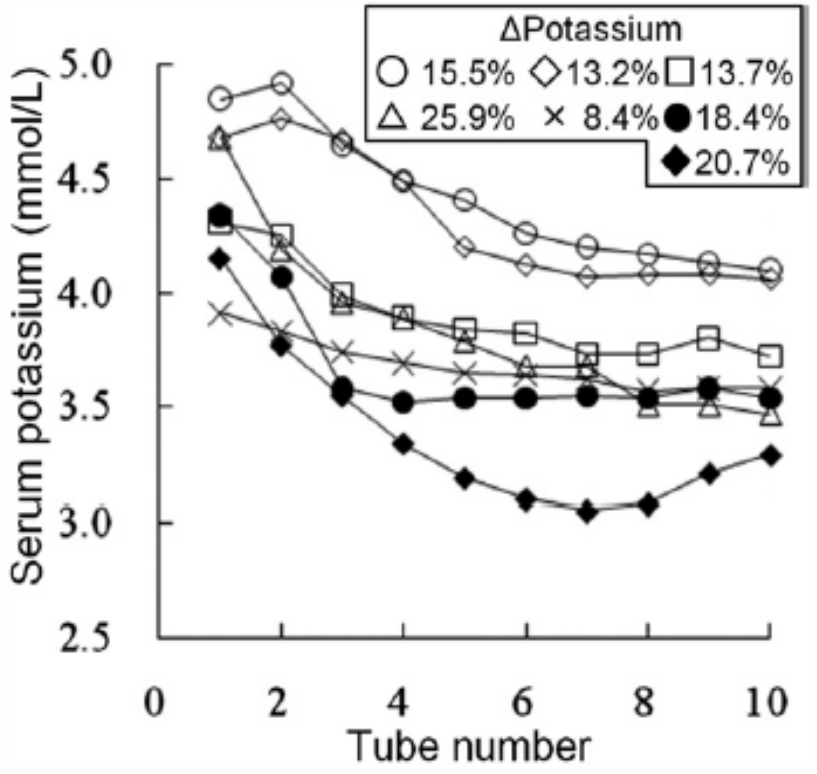


Figure 2. Time course of serum potassium levels after repeated fist clenching. After the last fist-clenching movement, serial blood samples (1 mL each) were obtained at 10-second intervals during application of a tourniquet. Abbreviation: Δ potassium, percentage of change in serum potassium level between the 1st and 10th tubes.

Seimiya M et al. Am J Kidney Dis 2010;56:686-92.

Tourniquet Time and Hemolysis

Table 1 Summary of data obtained from the proforma and results of statistical analysis showing exact *P* values for parameters studied

Parameter	Number of samples	Haemolysed	Exact *P* value (χ^2)
Staff group performing venepuncture			
Allied health professional	224	8 (3.6%)	0.006
Nursing	71	10 (14.1%)	
Medical	51	5 (9.8%)	
Unknown	*7*	*0*	
Method of sampling			
Butterfly	47	2 (4.3%)	0.008
Needle and syringe	31	1 (3.2%)	
Vacutainer	214	10 (4.7%)	
Venflon	60	10 (16.7%)	
Unknown	*1*	*0*	
Tourniquet time			
≤ 1 min	234	3 (1.3%)	<0.001
>1 min	99	20 (20.2%)	
Unknown	*20*	*0*	
Number of attempts at venepuncture			
1	288	16 (5.6%)	0.041
>1	31	5 (16.1%)	
Unknown	*34*	*2 (5.9%)*	
Mode of transport to laboratory			
Vacuum tube	298	22 (7.4%)	0.055
Hand delivery	47	0	
Unknown	*8*	*1 (12.5%)*	

Saleem S et al. Ann Clin Biochem 2009;46:244-246.

Forearm Exercise

Table 1. Effect of Stasis and Forearm Exercise on Local Venous Plasma Potassium, Bicarbonate, and Lactate Levels, Blood pH, and Partial Pressure of Carbon Dioxide (pCO_2).

Maneuver	Time	Potassium	pH	pCO_2	Bicarbonate	Lactate
	min	*mmol/liter*		*mm Hg*	*mmol/liter*	
Control	−2	3.8	7.36	46.6	25.5	0.80
	0	3.9	7.36	45.6	24.9	0.64
Tourniquet alone	1	3.9	7.36	45.2	24.9	0.82
	2	3.9	7.36	46.8	25.7	0.73
Tourniquet with clench	3	5.0	7.36	47.2	25.7	1.34
Recovery	4	3.8	7.29	56.8	25.7	1.93

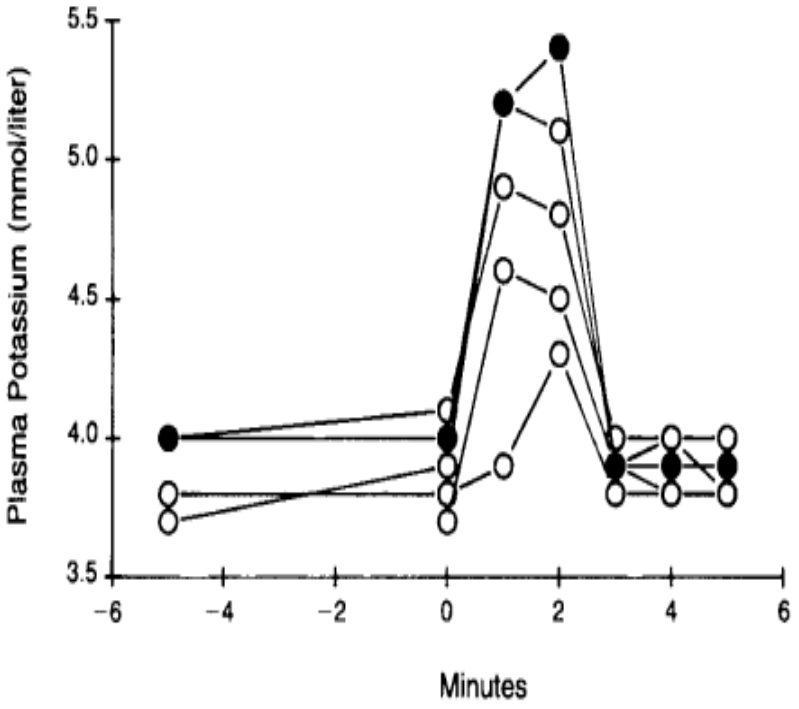


Figure 2. Effect of Handgrip Exercise on Plasma Potassium Concentrations.

Solid circles represent the patient, and open circles the control subjects. Handgrip exercise, which was maintained between minutes 0 and +2, increased plasma potassium levels in both the patient and the control subjects.

Don BR et al. N Engl J Med. 1990;322:1290-2.

Transportation

Pseudohyperkalemia due to pneumatic tube transport in a leukemic patient.

Table 1. Potassium Results of Specimens Handled by Different Methods to Determine Cause of Pseudohyperkalemia

Sample No.	Time Drawn	Potassium (mEq/L)	Method
1	12:16 PM	6.6	V, H/L, PT
2	12:15 PM	3.2	S, H, W (ICU)
3	12:39 PM	2.3	V, H/L, W
4	12:41 PM	2.5	S, H, W
5	12:43 PM	2.6	S, H/L (gentle pour), W

NOTE. Only the specimen (no. 1) sent in the pneumatic tube showed an elevation in plasma potassium level. To convert potassium in mEq/L to mmol/L, multiply by 1.

Abbreviations: V, vacutainer; H, heparin; L, lithium; PT, pneumatic tube; W, walked; ICU, intensive care unit.

Kellerman PS et al. Am J Kidney Dis 2005;46:746-8.

Pseudohyperkalemia due to pneumatic tube transport in a leukemic patient.

Table 2. Potassium Results in Simultaneous Specimens Obtained From the Patient on 2 Different Days and From Controls

	Potassium (mEq/L)	
	Tube-Transported	Walked
Patient	6.6	3.2
	10.3	5.1
Controls	4.7	4.9
	4.1	4.0
	3.8	3.7
	4.4	4.8
	5.1	4.9

NOTE. Controls are patients with normal WBC counts ($<10 \times 10^3/\mu L$ [$\times 10^9/L$]). To convert potassium in mEq/L to mmol/L, multiply by 1.

Kellerman PS et al. Am J Kidney Dis 2005;46:746-8.

Pseudohyperkalemia due to pneumatic tube transport in a leukemic patient.

Table 1 Measured K, AST and LDH concentrations, obtained in different specimens, using different transport routes

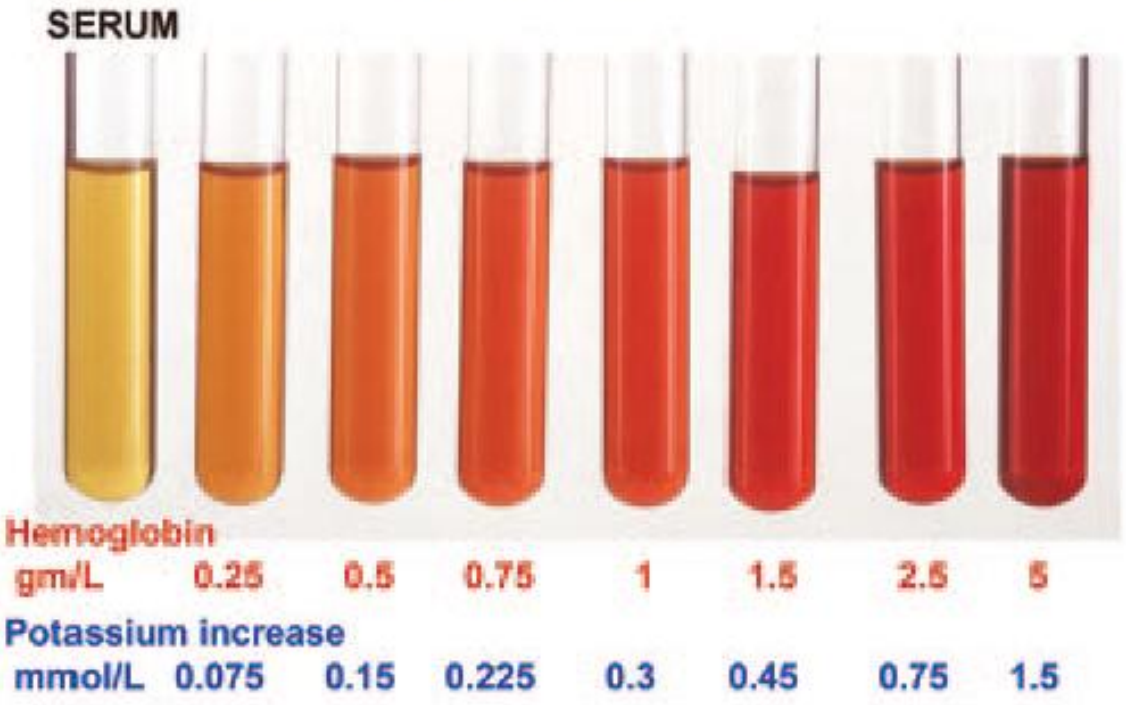
Date	Day 1			Day 3			Day 6			Day 9		
Analyte	K	AST	LDH	K	AST	LDH	K	AST	LDH	K	AST	LDH
Pneumatic transport												
Lithium-heparin tube	9.5	48	4732	6	39	2992	4.5	22	1487	3.4	16	830
Tube without anticoagulant	4.3	22	2233	4.1	25	1809	4	18	1159	3.4	18	774
Pedestrian transport												
Lithium-heparin tube	5.4	38	3435	3.5	20	1666	3.6	19	1168	3.2	15	782
Tube without anticoagulant	4.3	25	2302	3.9	19	1523	4	17	1148	3.4	17	744
Point of care analysis												
Lithium-heparin tube	nr	nr	Nr	3.5	nr	nr	3.7	nr	nr	3.1	nr	nr
Haemolysis index	0			0			0			0		
WBC, 10^9 cells/L	297			198			85			24.5		

K (mmol/L), AST (UI/L), LDH (UI/L) concentrations and haemolysis index (semi-quantitative results) were determined on an Advia 2400 analyser; point of care analysis used i-STAT analysers; WBC was measured on a Sysmex XE-2100 analyser (Sysmex Corporation, Kobe, Japan); nr: no result Reference range for K: 3.5–5 mmol/L, AST: 15–40 UI/L, LDH: 220–480 UI/L and WBC: 4–10 × 10^9 cells/L, K, potassium; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; WBC, white blood cell

Guiheneuf R et al. Ann Clin Biochem. 2010;47(Pt 1):94-6.

Hemolysis

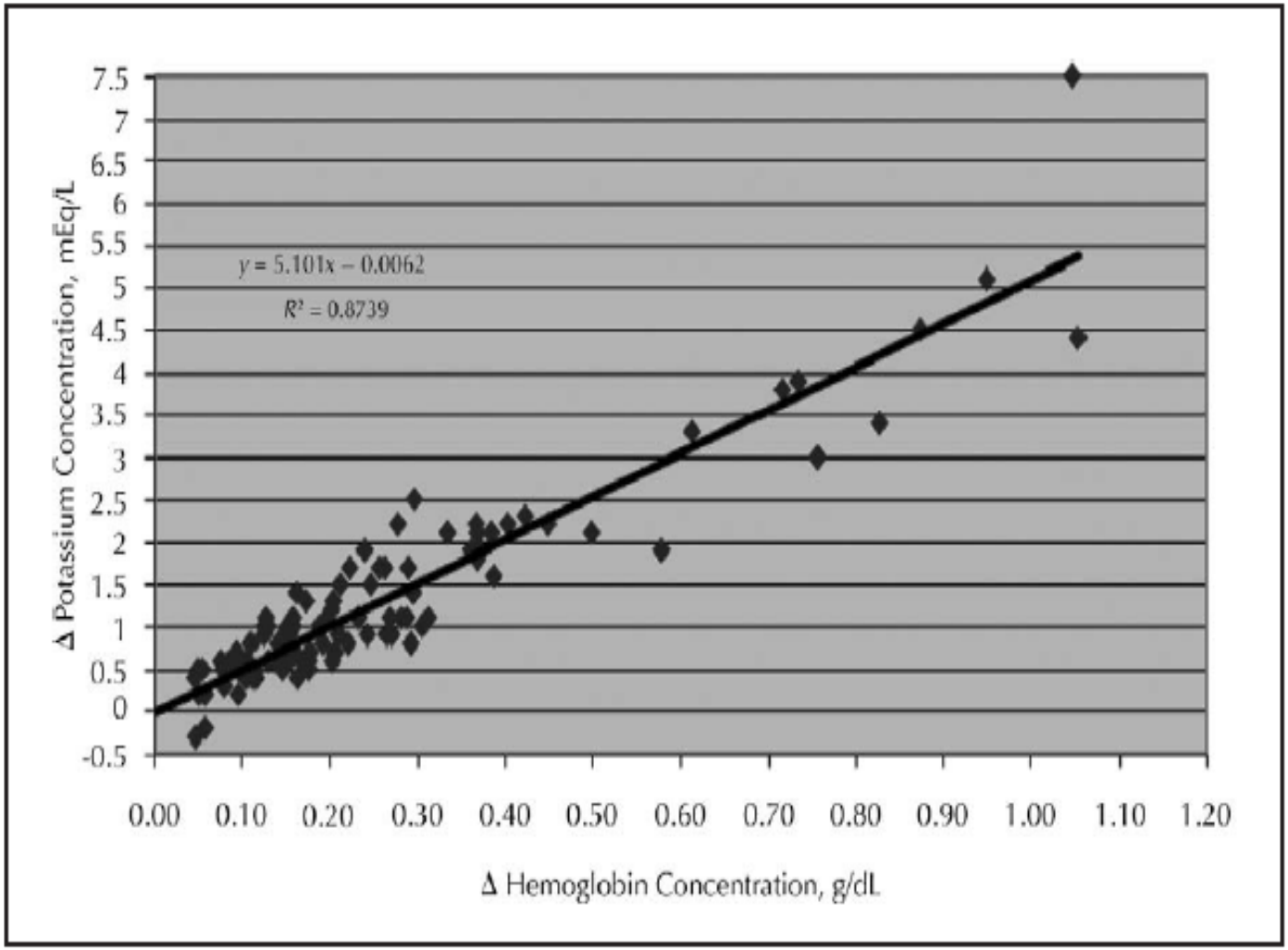
Figure 1. Hemolysis and its effect on potassium.



Hemolysis produced by adding increasing amounts of red cell hemolysate to a serum pool in a 19 X 75mm tube. The potassium increase is an average value expected. This cannot be used to correct the potassium value for hemolyzed specimens.

Baer Dm et al. MLO 2006 Nov.24-31.

Plasma hemoglobin concentration and increment in potassium concentrations



Mechanical hemolysis induced and potassium measured on Hitachi 747 analyzer

Mansour MM et al. Arch Pathol Lab Med 2009;133:960-966.

Hemolysis on potassium concentration

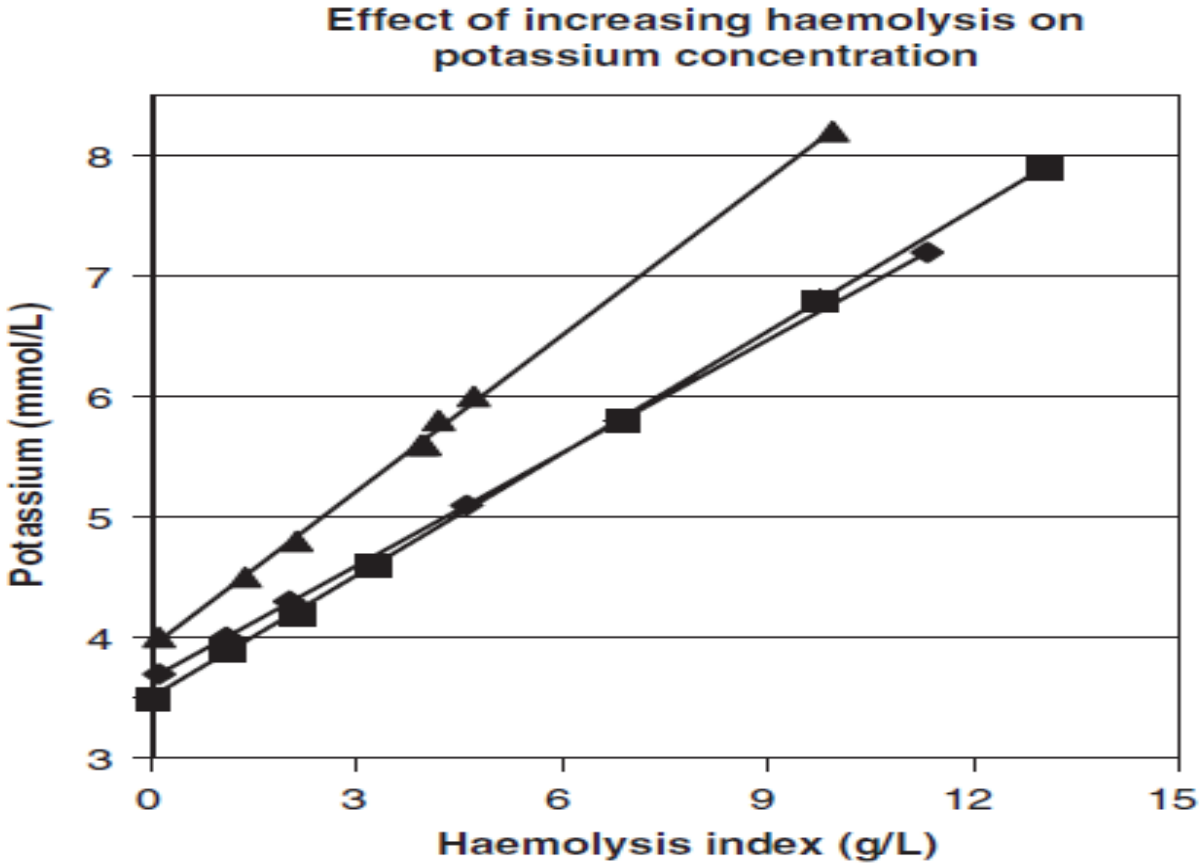


Figure 1. *Example of the effects of increasing haemolysis on potassium concentration with varying leucocyte count (■ 3.0 × 10⁹/L; ◆ 10.8 × 10⁹/L; ▲ 85.6 × 10⁹/L).*

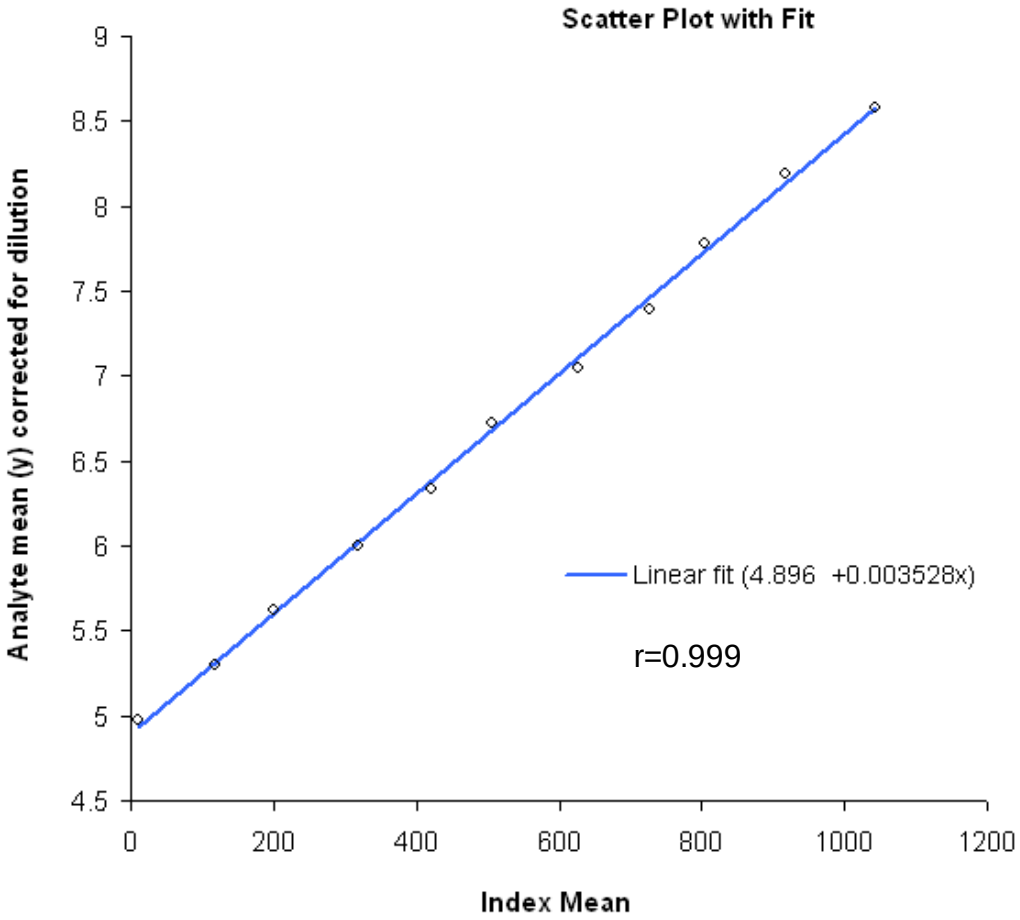
Mechanical hemolysis induced and potassium measured on Roche Sysmex 9000

Dimeski G et al. Ann Clin Biochem 2005;42;119-123.

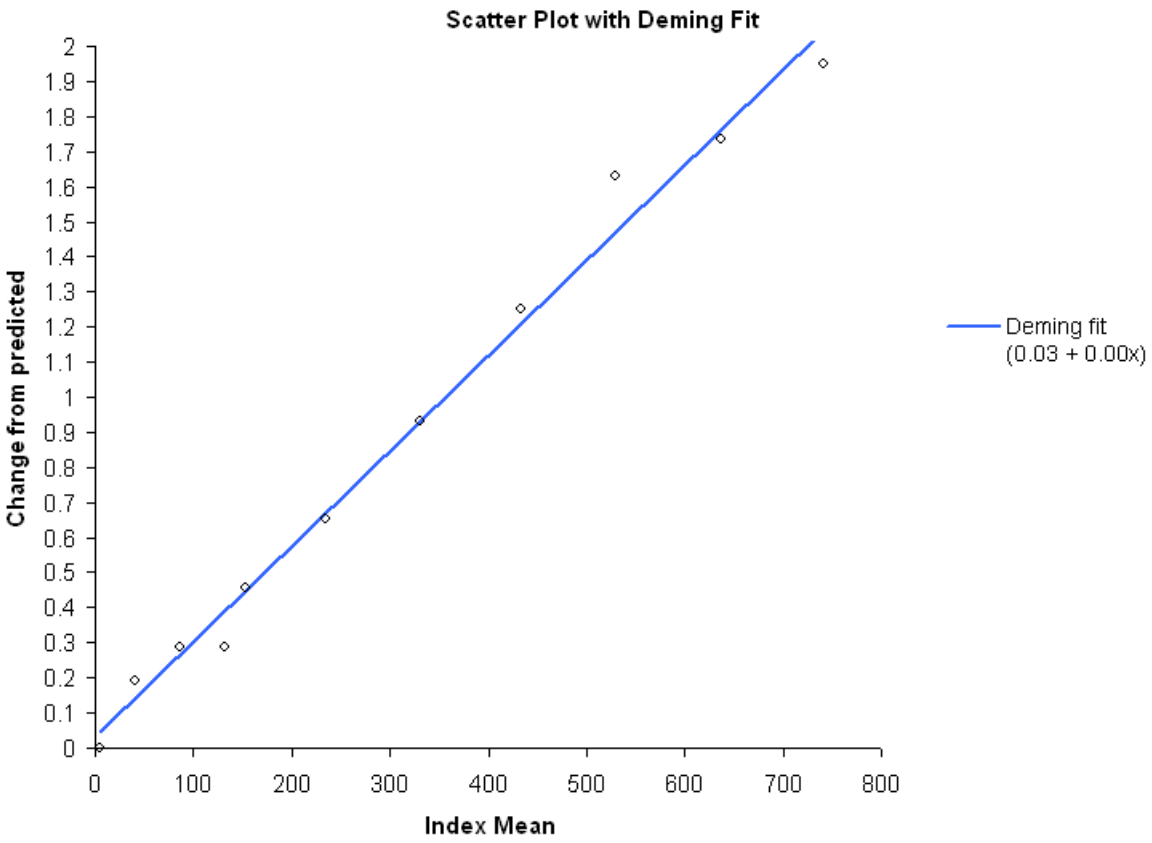
Hemolysis on potassium

Sample (x)	Analyte Mean (y)	Index Mean	Analyte mean (y) corrected for dilution	% change from baseline
Baseline	4.97	10	4.97	
Level 1	5.25	118	5.30	7
Level 2	5.51	200	5.62	13
Level 3	5.83	318	6.00	21
Level 4	6.10	422	6.34	27
Level 5	6.40	507	6.72	35
Level 6	6.65	628	7.05	42
Level 7	6.91	728	7.39	48
Level 8	7.21	805	7.78	56
Level 9	7.52	917	8.19	65
Level 10	7.80	1045	8.58	72

Hemolysis on potassium



Hemolysis on potassium



Baseline potassium 3.9 mmol/L

Royal University Hospital

Storage and Temperature

- If a whole-blood specimen is stored:

  At 25ºC: Serum potassium increase 0.2 mmol/L/1.5 hours (Goodman JT et al. Am J Clin Pathol 1954;24:111-113)

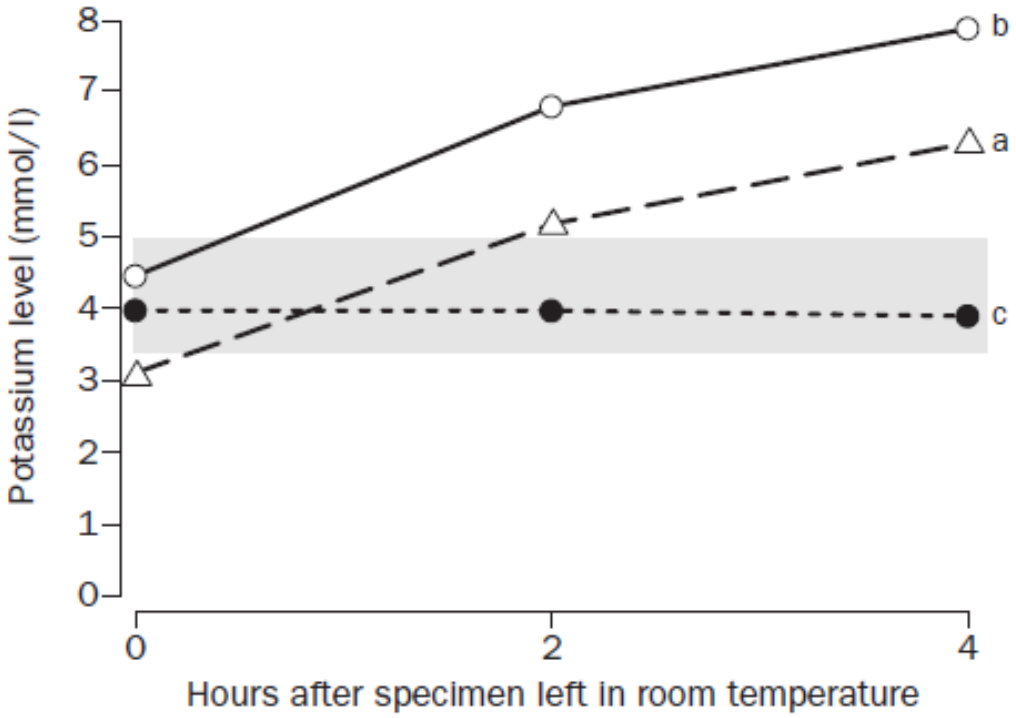
  At 4ºC: The increase is greater and 2 mmol/L after 5 hours (Oliver TK et al. Pediatrics 1966;38:900-902.). Mainly due to inhibition of glycolysis of RBCs and Na^+-K^+ ATPase

- The opposite effect of high temperature (37ºC) is a falsely decreased potassium due to increased glycolysis and intracellular shift of potassium.

- Ideal temperature for storage: 25-32ºC and centrifugation within 1 hour of collection

- Serum potassium remains stable in 3 hours and the serum should be separated from the clot within 3 h for potassium (Zhang DJ et al. Clin Chem.1998;44:1325-33.).

Changes in potassium levels in delay analysis



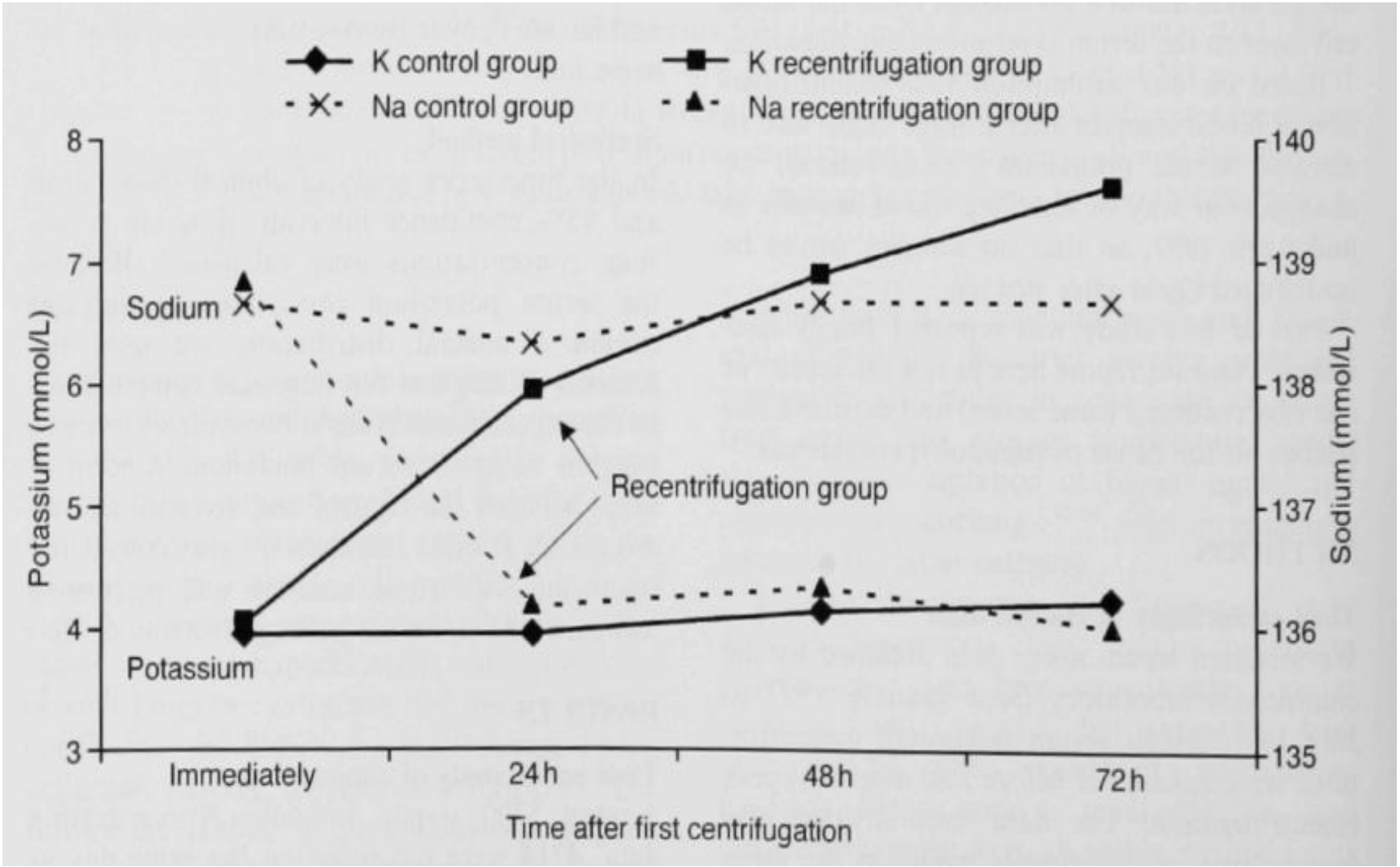
Changes in potassium levels
a: patient on potassium-lowering treatment; b: patient off potassium-lowering treatment; and c: father of the patient. Normal range of potassium level is shaded.

- 35-yr-old man was admitted with elevated potassium 7.3 mmol/L
- Repeated 7.8 mmol/L asymptomatic, normal blood count normal ECG.
- insulin-glucose infusion given to correct hyperkalemia
- Immediate measurement 3.1 mmol/L but rose steadily when sample was left at RT (blood gas).

Avoid life-threatening treatments

Vaidya et al. A Race to the Lab. The Lancet 2002;359:848

Recentrifugation and Pseudohyperkalaemia



Blood samples stored in serum separator tube gel can protect potassium leakage from cell layer to serum layer. Specimens to be tested for potassium should avoid respinning after 2 hrs collection.

Hira K et al. Ann Clin Biochem. 2001;38:386-90.
Hira K et al. N Engl J Med. 2000;343:153-4.

Paeudohyperkalemia in leukocytosis

- A 20-year-old female presented with chronic myeloid leukemia with a leukocyte count of 349.4 x 10^9/L and hyperkalemia.

- Morning of day 1:
  serum K = 12.4 mmol/L
- Afternoon of day 1:
  serum K = 9.6 mmol/L

- The underlying mechanisms:

- In leukemia, the leucocytes have abnormal fragility and this leads to potassium release when exposed to mechanical stress
- Severe leukocytosis will have higher consumption of metabolic fuels that may lead to impaired Na/K ATPase pump activity resulting in decrease of shifting potassium into cells.

Jacobsz M. SA Fam Pract 2007;49(7): 50.
Colussia G et al. *Am J Nephrol* 1995;15:450-2.
Kim A et al. Cases Journal 2010;25:3:73

Spurious hyperkalaemia associated with severe thrombocytosis and leukocytosis

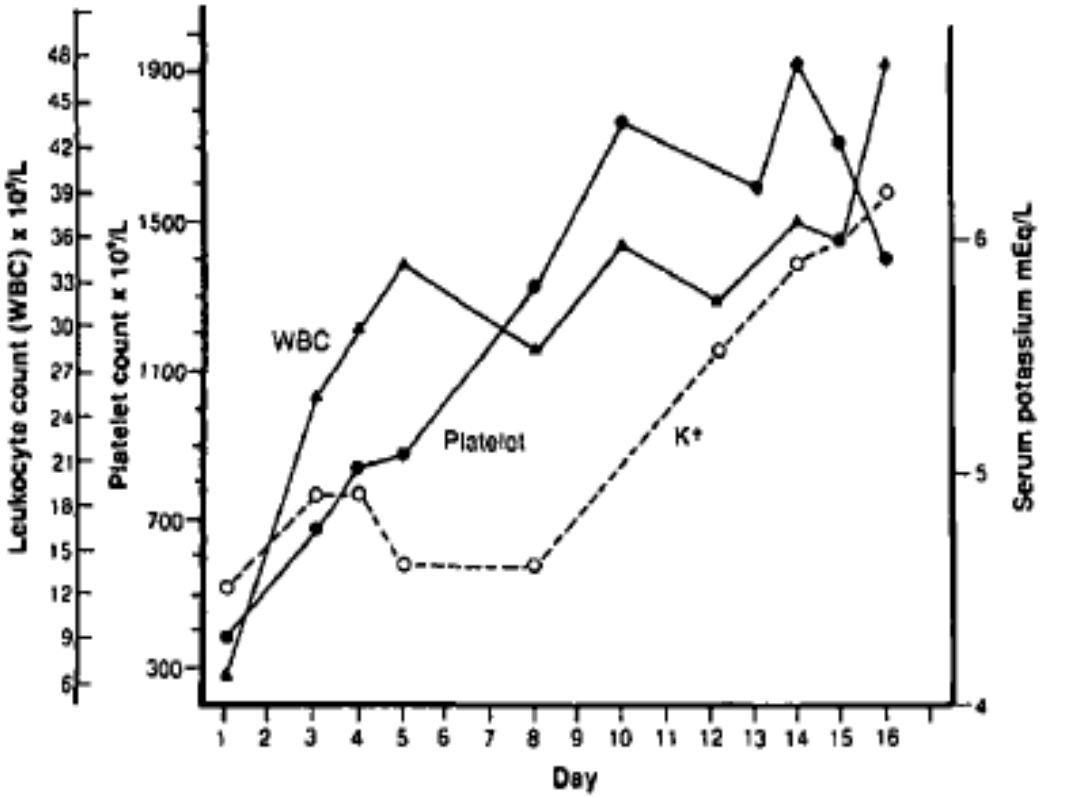


FIGURE The patient's blood platelet and leukocyte counts, and serum potassium concentration.

Ho AM et al. Can J Anaesth. 1991;38:613-5.

Elevated Platelets and Pseudohyperkalemia

The relationship between platelet levels and serum potassium concentrations

Patient and diagnosis	Platelet-rich plasma		Whole blood		Platelet-free plasma	
	Platelets ($\times 10^3$) *per cu. mm.*	Serum potassium *mEq./L.*	Platelets ($\times 10^3$) *per cu. mm.*	Serum potassium *mEq./L.*	Platelets ($\times 10^3$) *per cu. mm.*	Serum potassium *mEq./L.*
A. Patients with thrombocytosis						
M. H. Myeloid metaplasia (?)	3,120	9.6	1,210	7.2	<1	5.2
	3,470	8.8		7.8	<1	5.0
	3,220	8.0			<1	5.4
	1,610*	7.0				
	3,250	8.6			<1	4.2
	406*	4.8				
	102*	4.3				
	4,350	9.6				
D. Normal subjects						
S. M.	462	4.6			<1	3.9
R. H.	172	4.4	146	4.3	<1	4.5
E. N.	349	5.0	201	5.0	<1	5.3
J. G.	381	4.5	180	4.5	<1	4.6
L. C.	506	4.0	150	3.5	<1	3.6

* To obtain these levels the platelet-rich plasma was diluted with an appropriate amount of platelet-free plasma.

Hartman RC et al. J Clin Invest 1958;37:699-707.

Pseudohyperkalemia and platelet count

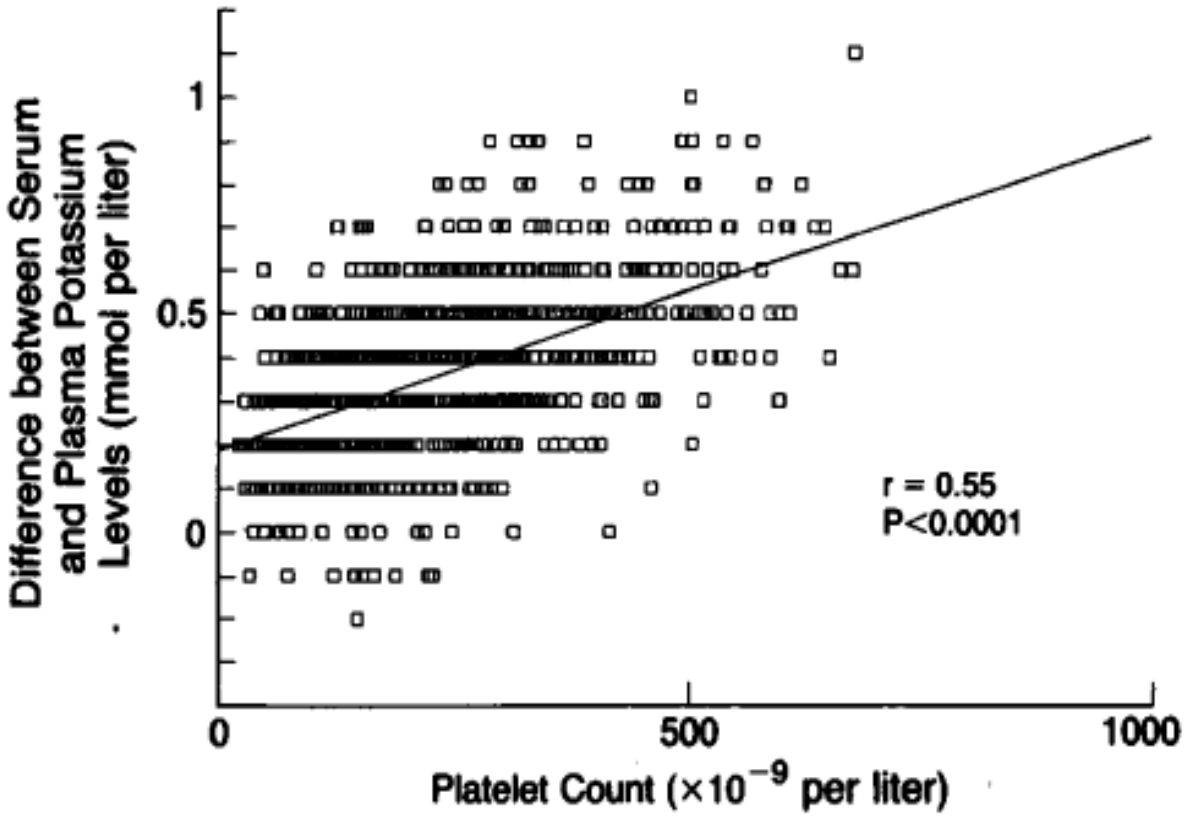


Figure 1. Relation of the Platelet Count with the Difference between Serum and Plasma Potassium Levels.

The mean serum and plasma potassium difference is 0.36 ± 0.18 mmol/L (0.2-0.5mmol/L, up to 2.61 mmol/L). The increase of 0.73 mmol per 10^{12} platelets.

Nijsten MW et al. N Eng J Med 1991;325:1107.

Pseudohyperkalemia and platelet count

- The incidence of hyperkalemia was 34% in patients with over 500 x 10^9 platelets/L compared with 9% if the platelet count was below 250 x 10^9/L (Graber M et al. Am J Kidney Dis 1988;12:116-20).

- Serum potassium rises in direct proportion to the platelet count in normal patients and in those with thrombocytosis (Graber M et al. Am J Kidney Dis 1988;12:116-20)

- An increase of **1,000** x **10^9** /L in blood platelet count (Ref Range:150-400x10^9 /L) would cause an increase of about 0.2 mmol/L in plasma potassium and **0.7** mmol/L in **serum** potassium (Nijsten MW et al. N Eng J Med 1991;325:1107. Makela K et al. Scand J Clin Lab Invest Suppl. 1995;222:95-100).

- Pseudohyperkalaemia was observed in patients with Kawasaki disease showing remarkably increased platelet counts.

- Pseudohyperkalemia in Postsplenectomy Thrombocytosis

Pseudohyperkalemia and Erythrocytosis

Table 3. Characteristics and Laboratory Findings of Patients in Phase Two[a]

Clinical settings	n* m/f	Age (years)	Hct (%)	WBC ($\times 10^3/\mu l$)	Plt ($\times 10^3/\mu l$)	Sk (mmol/L)	Pk (mmol/L)	Dk (mmol/L)
Polycythemia vera	19/16	64 (11)	54 (51–59)[b] 52 (46–61)[c]	13 (6–35)	596 (294–4000)	4.94 (4.29–6.81)	3.96 (3.30–5.39)	0.98 (0.71–2.31)
Erythrocytoses	37/18	59 (10)	54 (51–61)[b] 52 (46–58)[c]	7 (4–31)	282 (47–650)	4.49 (3.49–5.30)	4.10 (2.95–4.90)	0.41 (0.23–0.62)
Spurious erythrocytosis	25/7	62 (10)	53 (46–60)	7 (4–11)	286 (47–484)	4.48 (3.49–5.30)	4.07 (3.26–4.90)	0.39 (0.23–0.56)
Chronic obstr. pulmonary dis.	10/8	57 (12)	55 (49–61)	6 (4–11)	250 (148–650)	4.54 (3.53–4.80)	4.10 (3.25–4.32)	0.47 (0.28–0.55)
Neoplasms	2/3	54 (7)	50 (48–55)	11(7–31)	418 (147–649)	4.29 (3.57–4.80)	3.84 (2.95–4.32)	0.48 (0.31–0.62)

[a] *Results are given as median (range), except for age, which is given as mean (SD).*
[b] *male.*
[c] *female.*
* *male/female.*
Dk, difference between serum and plasma potassium concentration; PK, plasma potassium concentration; SK, serum potassium concentration.

Sevastos N et al. Am J Med Sci 2006;331:17-21.

Familial Pseudohyperkalemia

- Familial pseudohyperkalemia is a condition in which the red blood cells show a temperature-dependent potassium leakage when stored at room temperature (leaky red cell syndrome).

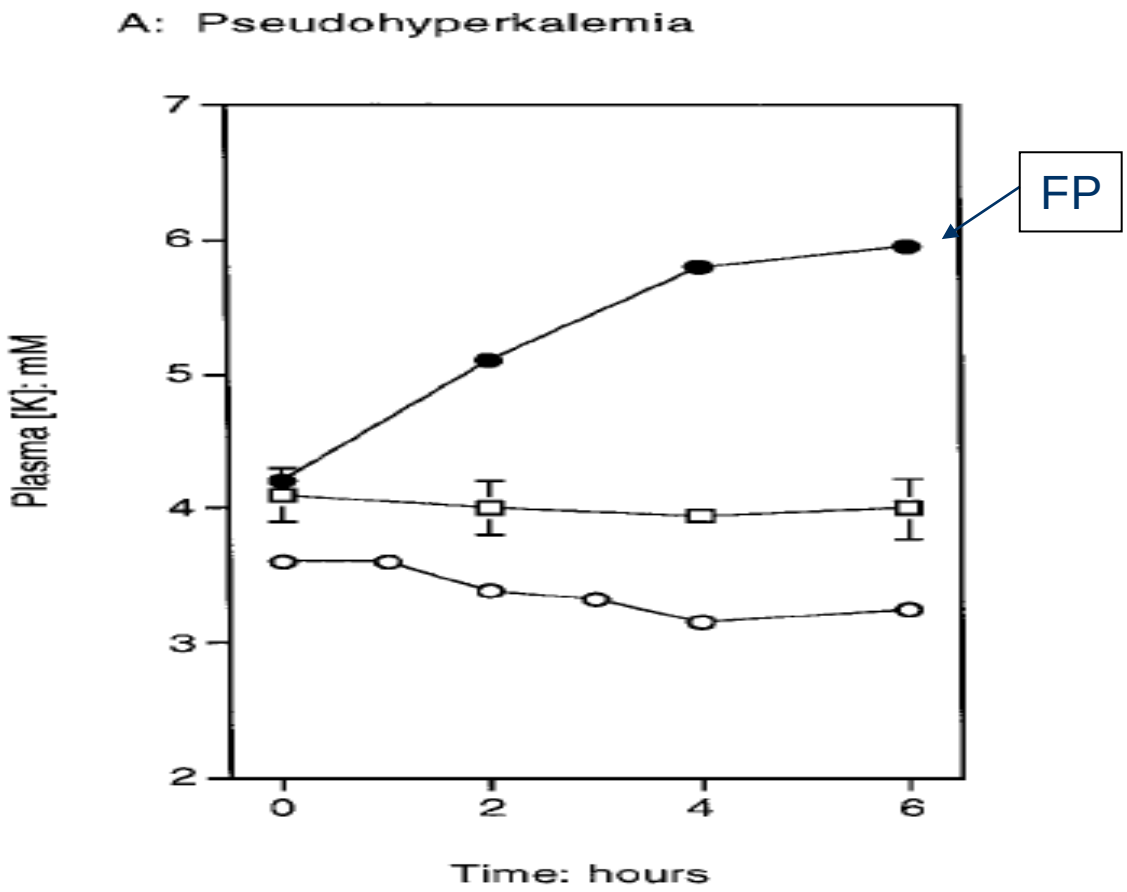
- Autosomal dominant disorder, a hereditary stomatocytosis.
  Such genetic defects with increased red cell membrane permeability are seen in dehydrated hereditary stomatocytosis (DHS) and overhydrated hereditary stomatocytosis (OHS).

- Affected subjects are not anemic and have normal in-vivo plasma potassium concentrations.

Stewart GW, Fyffe JA, Corrall RJM. Lancet 1979;2:175-7.
Iolascon A et al. Blood 1999;93:3120-3.
Grootenboer S et al. Blood. 2000;96:2599-605.

Familial Pseudohyperkalemia

- A case of dehydrated hereditary stomatocytosis (DHS) with pseudohyperkalemia



Heparin blood at room temperature for 6 hrs

Iolascon A et al. Blood 1999;93:3120-3.

Reverse Pseudohyperkalemia

- **Traditionally** pseudohyperkalemia is diagnosed when the SERUM potassium level exceeds the plasma potassium level by 0.4 mmol/L.

- **Reverse Pseudohyperkalemia** is defined as falsely elevated potassium levels in PLASMA samples compared to serum.

- The underlying mechanism is due to heparin-induced membrane damage in the face of a hematological malignancy.

Singh PJ et al. Miner Electrolyte Metab 1997;23:58-61.

Reverse Pseudohyperkalemia

- A 49-yr-old woman with chronic lymphocytic leukemia (CLL). Her WBC $364x10^9$/L, $100x10^9$ platelets/L. Her potassium from lithium heparin gel tube was 10.7 mmol/L and second specimen was 11.2 mmol/L on Beckman LX-20.
- Plasma potassium concentrations exceeded serum potassium concentrations by more than 1.3 mmol/L.

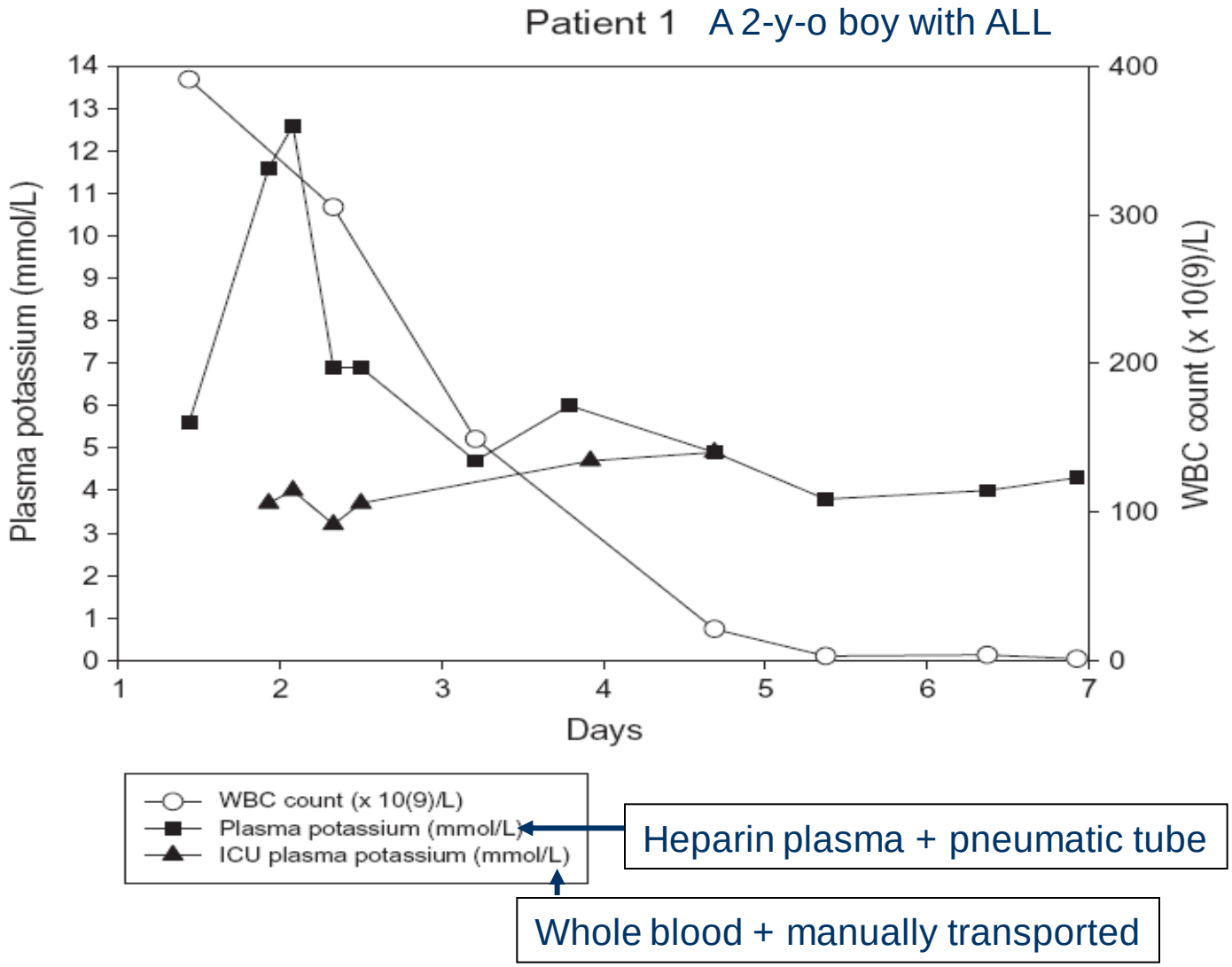
Table 1. Measured potassium concentrations obtained in different specimens drawn simultaneously.[a]

Specimen	Potassium concentration, mmol/L	Specimen type	Analyzer (method)
A	4.9	Plasma lithium-heparin without separator gel	Beckman LX-20 (indirect ion selective electrode)
B	4.0	Plasma lithium-heparin with separator gel	Beckman LX-20 (indirect ion selective electrode)
C	2.6	Whole blood lithium-heparin specimen	Rapid Lab 1200 (direct ion selective electrode)
D	2.7	Serum	Beckman LX-20 (indirect ion selective electrode)

[a] All specimens were kept at ambient temperature during transport, centrifugation, and analysis. The laboratory reference interval for adult plasma potassium concentration is 3.5–5.0 mmol/L.

Abraham B et al. Clin Chem 2008;54:449-51.

Reverse Pseudohyperkalemia



Garwicz D et al. Clin Chim Acta. 2011;412:396-7.

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Reverse pseudohyperkalemia in heparin plasma samples from a patient with chronic lymphocytic leukemia

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ABSTRACT

Objectives: To investigate the spurious high potassium results in heparin plasma.

Design and methods: Potassium values from heparin plasma, serum, and whole blood in a patient with chronic lymphocytic leukemia were determined and compared on chemistry and blood gas analyzers.

Results: Potassium levels were strikingly elevated in heparin plasma compared to serum or whole blood in which the potassium levels were surprisingly normal.

Conclusions: The phenomenon of reverse pseudohyperkalemia should be publicized.

Patients and methods

- An 86-year old woman with end stage of chronic lymphocytic leukemia (CLL).
- She was investigated for hyperkalemia in oncology, cardiology, and ICU for over 2 months and given insulin-glucose infusion to corret hyperkalemia.
- The patient's initial laboratory results were: WBCs 374 x 10^9 cells/L (96% lymphocytes) (4.00-11.00 x 10^9) and platelets 158 x10^9 platelets/L (150-400 x 10^9), RBC 2.13x10^{12}/L (3.20-5.40 x 10^{12}), creatinine 84 µmol/L (45-90), and LDH 382 U/L (reference range 120-230 U/L).
- Plasma potassium value was 7.5 mmol/L. Specimen was collected in 4.5 ml lithium-heparin Plasma Separator Tube (PST).
- Repeat measurement of potassium from the above plasma was 7.4 mmol/L. The same plasma specimen was also analyzed on ABL blood gas analyzer and the potassium value was 7.2 mmol/L.
- Potassium was 2.8 mmol/L from whole blood collected at the same time.

Results

Table 1
Potassium concentrations obtained from different types of specimens and analyzers.

Electrolytes (mmol/L)	Chemistry analyzer (Roche Cobas c501)	ABL gas analyzer
	Lithium-heparin plasma	Arterial blood
Sodium	141	140
Chloride	94	94
Potassium	7.5	2.8
Bicarbonate	42	39

Meng QH et al. Clin Biochem 2011;44:728-30.

Results

Table 2
Comparison of potassium values from different types of specimens measured on different analyzers.

Type of specimen	Potassium (mmol/L)	LDH (U/L)	Analyzer (method)
Lithium–heparin plasma without separator gel	10.94	402	Roche Cobas c501 (indirect ISE*)
Lithium–heparin plasma with separator gel	10.0	792	Roche Cobas c501 (indirect ISE)
Lithium–heparin venous whole blood (tube)	9.7	ND	ABL725 (direct ISE)
Serum	4.7	317	Roche Cobas c501 (indirect ISE)
Venous whole blood (balanced lithium–heparin syringe)	4.3	338	ABL725 (direct ISE)

* ISE: ion selective electrode, LDH was measured on Cobas analyzer, ND: not determined.

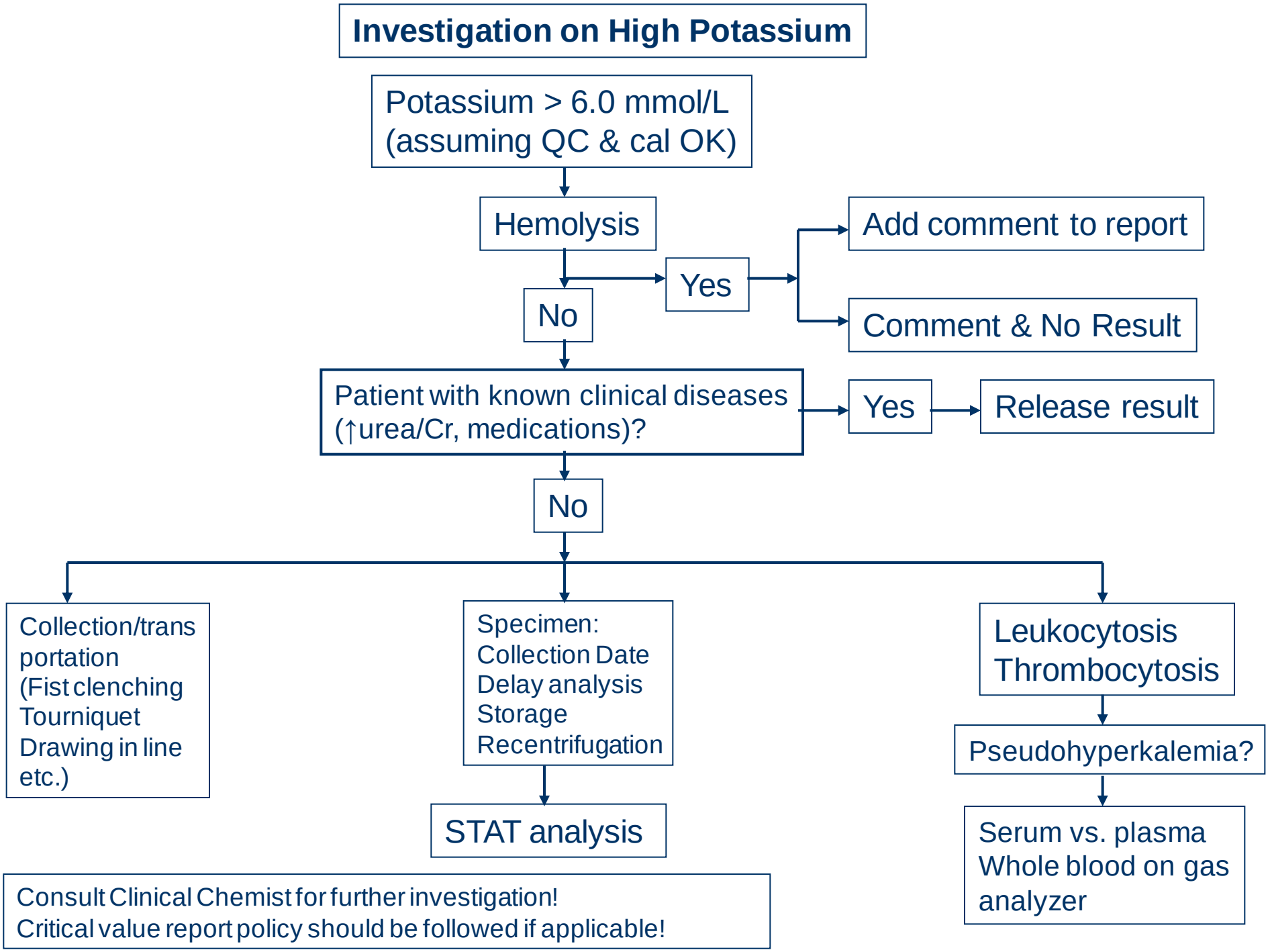
Meng QH et al. Clin Biochem 2011;44:728-30.

Discussion and Conclusions

- Our findings support the heparin-induced leakage of potassium from WBCs.
- When pseudohyperkalemia suspected, prompt centrifugation and assay should be performed to avoid hemolysis and the delay of analysis.
- The presence of pseudohyperkalemia should be suspected in any patient with marked leukocytosis or thrombocytosis. Simultaneous measurements of serum and plasma potassium levels should be performed to compare the difference.
- For reverse pseudohyperkalemia in heparinized plasma in patients with leukocytosis, a whole blood specimen collected in balanced heparin syringe should be analyzed on the blood gas analyzer or serum potassium is also recommended.
- Lack of typical ECG changes may be helpful in pseudohyperkalemia.
- High plasma LDH may indicate hemolysis or rupture of fragile WBC.

Differential Diagnosis

Differntial Diagnosis	Serum K^+	Plasma K^+	Others
Hyperkalemia	↑	↑	ECG
Pseudohyperkalemia	↑(falsely)	Normal	No ECG
Reverse pseudohyperkalemia	Normal	↑(falsely)	No ECG
Tumor lysis syndrome	↑	↑	ECG change ↑ Uric acid ↑ Phosphorus ↓Calcium


Investigation on High Potassium
Potassium > 6.0 mmol/L
(assuming QC & cal OK)
Hemolysis
Yes
Add comment to report
Comment & No Result
No
Patient with known clinical diseases
(↑urea/Cr, medications)?
Yes
Release result
No
Collection/trans
portation
(Fist clenching
Tourniquet
Drawing in line
etc.)
Specimen:
Collection Date
Delay analysis
Storage
Recentrifugation
STAT analysis
Leukocytosis
Thrombocytosis
Pseudohyperkalemia?
Serum vs. plasma
Whole blood on gas
analyzer
Consult Clinical Chemist for further investigation!
Critical value report policy should be followed if applicable!

Thank You!