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Spurious Test Results in Blood Sampled from Venous Lines

Jochanan E Naschitz, MD, Mor Rivka Levy, BA, MA, RN, Ricky Cohen, BA, MPH, PhD and Bahaa N Francis, MD, MSc, PhD, MRCP, MHA

Bait Balev Nesher and The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel.

***Correspondence:**

Professor emeritus Jochanan E Naschitz, MD, Bait Balev Nesher and The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel, Tel: 050-8573244, Fax 97248345575.

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ABSTRACT

Spurious blood test results are technically correct but do not match the person's clinical data. Because of this spurious blood test results may be a source of confusion and sometimes harm. The causes of spurious test results from samples drawn from venous lines or by venipuncture may differ. The former arises, essentially, by two mechanisms: 1. dilution of the blood contained in the line by infusate treatment or by fluid used for locking the line, and 2. by adhesion of molecules or particles to the inner surface of the line. Illustrative case histories are presented featuring tests results in blood drawn from venous lines: spurious extreme hyponatremia, spurious steep drop of hemoglobin concentration, and spurious toxic plasma vancomycin. A threefold message emerges from these observations. First, blood samples for analyses should be obtained by direct venipuncture as a norm. Second, when a venous line is already in use it may also serve for blood sampling provided an appropriate fluid volume is discarded from the line before the sample is drawn for analysis. Third, in facing an unusual or improbable laboratory result the test should be double checked by venipuncture. The cause of the inaccuracy should be exposed and avoided in the future.

Keywords

Blood tests, Spurious, Venous line, Cannula.

Introduction

Spurious blood tests are inaccurate results not corresponding to a person's clinical condition. They may mislead the diagnosis and treatment. The gamut of spurious test results in blood drawn by venipuncture includes blood counts, serum electrolytes, coagulation tests, glycemia, hormone levels, bacteriological assays, antibiotic plasma levels, and oxygen saturation [1-6]. Most errors occur in the preanalytical phase, due to inappropriate sample volume, hemolysis, clotting, contamination by infusion fluids, wrong container (cross-contamination of tube additives, or inappropriate sample storage [6]. In drawing blood from a venous line additional sources of error are introduced, essentially by two mechanisms: 1. dilution of the blood within the line, and 2. adhesion of molecules or particles to the inner surface of the line.

There is paucity of data in the literature concerning spurious blood test results in samples drawn from venous lines. Out of 342 titles concerning spurious blood test (in general) found on PubMed by December 2025, a search under the headings spurious blood test linked with either venous line, venous cannula, central line, PICC, retrieved but 1 to 5 titles, each. Use of a checklist was efficient for improving sample quality. The main points in the checklist are verification of the blood collection devices, patient preparation, verification of sampling techniques [5]. Errors related to sampling blood from venous lines may be prevented simply by direct venipuncture. Indeed, sampling blood from venous lines should be avoided "except once, at line insertion" [6]. Yet, when lines are already in use for administration of medications and fluids, sampling blood from venous lines is often used. Sampling blood for analyses from venous lines is an acceptable alternative to venipuncture if correctly done and the results of both tests are

equivalent. Previous studies had found agreement between the two methods for sodium, chloride, urea, creatinine and hematology samples, but not for potassium [7] and for mean corpuscular volume and mean corpuscular hemoglobin concentration [8]. Spurious blood results in samples collected from venous lines continue to happen, as illustrated in the following. Blood sampling technique from venous lines deserve notice.

Spurious blood test results by hemodilution

Case 1: Pseudohyponatremia in Extremis

Nonadherence to the rule of discarding the waste retained in the venous line before drawing the blood sample may cause particularly aberrant results, as illustrated in the following observation. An 87-year-old woman was admitted to the geriatric hospital for rehabilitation, having experienced 2 weeks earlier an ischemic stroke. At the time of admission, she was in hemodynamically stable condition (supine blood pressure 112/60 mmHg, heart rate 79 bpm, oxygen saturation 94%), but with poor cognition, disordered behavior and low food intake. Orthostatic hypotension was diagnosed. Remarkable in her medical history were ischemic heart disease, chronic atrial fibrillation, and dementia. In the ward she received oral nutrition according to a refeeding protocol, vitamins B supplements, intravenous fluid and electrolytes as needed. Her medications were bisoprolol fumarate, apixaban, furosemide, quetiapine, Easy-meal, and laxatives. Infusion of 1000 mL glucose 5% was started due to a borderline low glycemia. On the seventh day in hospital the patient lost consciousness while sitting in a reclining wheelchair. Her pulse was barely palpable, the blood pressure was 48/34 mmHg. She was hurried to bed where she regained consciousness instantly; her supine blood pressure returned to usual levels. The blood sugar sampled at this time by finger prick was 96 mg/dL. A simultaneously drawn through indwelling venous line sample showed glucose of 759 mg/dL and sodium 114 mEq/L. Obviously, the immediately before discontinued 5% glucose infusion was responsible for the high glucose and the low sodium in this sample, i.e. pseudohyponatremia. During the subsequent days the patient's laboratory tests via venipuncture were unremarkable (Table 1). The syncopal event was attributed to orthostatic hypotension. Finally, there was no recurrence of syncope but no significant improvement in her general condition. She was transferred to a nursing home for compassionate care.

Table 1: Blood chemistry results before, during and after the syncopal event.

Blood tests	Reference range	April 27	April 28	May 4 *	May 5
Glucose mg/dL	70- 100	111	83	759	74
Sodium mEq/L	136 - 146	141	140	114	138
Potassium mEq/L	3.5 – 5.1	3.3	3.2		3.1
Creatinine mg/dL	0.5- 1	1.01	1.16		1.1
BUN mg/dL	12- 22	24	28		21

*The blood sample drawn in emergency did not suffice for complete chemistry examination.

Severe hyperglycemia in the sample collected from the venous line contrasts with normal glycemia in the concurrently drawn capillary blood. Likewise, the time course of natremia, before and after the event, demonstrates the spurious nature of hyponatremia in the given context. It illustrates the artifact caused by drawing blood through a venous line without discarding the waste contained in the line. In this patient, low sodium in a mixture of blood and infusion glucose differs from pseudohyponatremia in diabetic patients. The high serum concentration of glucose reduces the water phase in the sample [9], while in the aqueous phase of the sample the sodium concentration may be normal [10,11]. There are correction factors for serum sodium under hyperglycemia which are applicable for proper blood samples [12] but not for diluted samples as in our patient. Whatsoever, in her case there was no challenge for the interpretation of the very low natremia.

Case 2: Dramatic drop in Hemoglobin Concentration in the Absence of Hemorrhage

A 67-year-old woman was hospitalized in our institution for two years, receiving prolonged mechanical ventilation. She had a medical background of olivo-pontocerebellar atrophy, respiratory failure, oropharyngeal dysphagia, pulmonary aspirations, atrial fibrillation, anemia of chronic disease, hypothyroidism and recurrent urinary and respiratory infections. She received enteral feeding via gastrostomy. Her medications were amiodarone, apixaban, esomeprazole, levothyroxine, midodrine, and sodium valproate. The baseline blood pressure was 106/56 mmHg, the heart rate 66 bpm, her body weight was 44 kg; the hemoglobin level was 10 g/dL, MCV 92 fl, the transferrin saturation 21%, eGFR 64 ml/min/1.73m2. During the preceding months she developed twice severe sepsis along with a remarkable drop of hemoglobin concentration. The latest event is briefly described, as presented with fever 39^{0}C, sweats, hypoactive delirium and arterial hypotension. Blood and urine cultures were retrieved and empirical treatment was started with ceftriaxone, hydration by intravenous isotonic saline and water by gastrostomy. The urine culture grew Klebsiella pneumoniae. Within 32 hours of antibiotic treatment the body temperature returned to normal along with the other vital signs. Intriguing was a dramatic decline of hemoglobin concentration concurrently with sepsis. There was no evidence of gastrointestinal or other bleeding. The serum haptoglobin, bilirubin, creatinine, urea, sodium and potassium displayed minimal, clinically not meaningful changes. The course of relevant laboratory tests during this period is shown in Table 2.

Several factors may be accountable for the steep fall of the patient's hemoglobin level in the context of sepsis: anemia of sepsis, systemic hemodilution by administration of large volumes of saline and water, in situ hemodilution in the venous line where saline infusion was delivered and where blood was drawn for laboratory tests. Intriguing also was the rapid restoration of hemoglobin to baseline level, increasing from 6.4 to11.2 g/dL over one day, after only one unit of packed red blood cells was transfused. Indeed, administration of one unit of packed red blood cells is expected to increase the hemoglobin concentration by approximately 1 g/dL [13].

Table 2: The course of anemia in the context of sepsis.

Test	Reference range	2 July	7 Aug	5 Sept*	7 Sept**	8 Sept	10 Sept	12 Sept
Hemoglobin g/dL	12.5 - 16	9	10.3	7.3	6.4	7.6	11.2	9.3
MCV fl	79 - 97	97	94	94	94	91	92	92
Neutrophils mcl/^{3}	1.8 -7.7	5.3	4.6	7	12.4	10.9	13.6	12.8
Iron mcg/dL	50 - 170	75	51	69	13	16	35	40
Transferrin mg/dL	250-38	206	168	107	114	122	158	137
CRP mg/dL	0 – 0.5	6.2	2.4	29.8	24.4	18.8	17.2	7.4

*Onset of fever and antibiotic treatment started, ** one unit of packed blood cells administered

First, 'anemia of sepsis' is diagnosed when anemia develops abruptly during sepsis and other causes are excluded. The pathophysiology is similar with anemia of chronic disease, either infectious, inflammatory or neoplastic; it is triggered by proinflammatory cytokines. Under action of proinflammatory cytokines, the hepatic production of hepcidin is increased. Hepcidin blocks ferroportin, the iron channel responsible for mobilization of iron from the reticuloendothelial system, inhibit erythropoiesis, and shorten red blood cell survival. The resulting anemia is characterized by low serum iron in the presence of normal or increased iron stores with transferrin saturation of 2-20% and MCV of 72-100 fl, not to be confused with iron deficiency anemia [14]. In a study of anemia in critical illness, at the time the patients were admitted to the intensive care unit anemia was found in 44% of cases, with a drop of the median hemoglobin concentration by 2 g/dL, which developed over a median of 1.2 days. In contrast to the quick development, resolution of the anemia after sepsis was slow; it was still noticeable 3 months after discharge [15]. At difference, quick fall and quick rise of hemoglobin concentration was noticed in our patient, taking only 2 days. This time course is not consistent with anemia of sepsis but is consistent with hemodilution.

Dilution of the blood sample by intravenous infusion of saline (or other crystalloid solution) results in a proportional decrease in the concentration of other constituents, except those included in the infused fluid. The 'rule of proportional decrease' was described in the remarkable observation of a patient with hematochezia, when the hemoglobin dropped from 13.3 g/dL (the first sample) to 6.7 g/dL (the second sample) under infusion of normal saline and without ongoing hemorrhage [16]. A third blood sample taken 4 hours later showed hemoglobin 9.7 g/dL. The discrepant hemoglobin values are explained in the context of infusion of normal saline. The second sample was obtained under infusion of normal saline; in this sample the white blood cells, potassium, creatinine and BUN had decreased in parallel with the decline of hemoglobin, demonstrating hemodilution. The third blood sample was obtained after discontinuation of saline infusion; the test showed increased white blood cells, potassium, creatinine and BUN in parallel with the increase in hemoglobin. A proportional decrease in the concentration of other blood constituents, except those included in the infused fluid, expresses the effect of hemodilution. A similar mechanism was probably involved in our patient, either by fluid administration or by saline retained in the venous line, thus diluting the blood drawn through the line on September 7 and 8, but later venipuncture only used. This explanation is supported by the parallel course of hemoglobin concentration and the concentration of other blood constituents (serum iron and transferrin), first the parallel decrease followed by their increase in parallel.

To minimize hemodilution artifacts when blood is drawn from a venous line, experts recommend that a volume of blood be discarded from the line before taking the blood sample for examination [17,18]. The minimum volume of blood to be discarded from the venous line for obtaining a valid sample may depend on the length and the caliber of the cannula. Studies have repeatedly addressed this issue and reached different conclusions [19-23]. Five mL of fluid exceeds the intraluminal volume of the usual cannula. Yet, in practice the discarded volumes differed: 6 mL for tunneled line, 9 mL for nontunneled line, 7.5 mL for blood culture, and 25 mL for coagulation profile [20]. In a study from intensive care units, the mean volume discarded from peripheral venous lines was 5.74mL (± 2.85), from peripheral access central line 7.34 mL (± 3.03) and from central venous catheter 6.49mL (± 2.99) [23].

Spurious blood test resulting from contamination of the venous line

Contamination of the blood samples may be due to adherence of chemicals or microbiota to the internal surface of the venous line, thereby polluting the sample.

Case 3: Falsely Elevated Plasma Levels of Vancomycin

We have previously reported the unusual observation of spurious toxic vancomycin levels in blood sampled from a venous PermCath line. The 56-year-old man with sternal osteomyelitis was treated with vancomycin 1 g/24 hours. The steady-state vancomycin plasma concentrations taken several times from the PermCath line were toxic level, 62–120 µg/ ml, while samples drawn from a peripheral vein were within the therapeutic range (about 10 µg/ml) [24]. After flushing the PermCath line with 50 mLof saline the vancomycin concentration in blood drawn from the line remained within toxic level. Yet, there were no signs of vancomycin toxicity and the plasma creatinine 0.8 mg/dL was in the normal range. Vancomycin administration was discontinued. Sixteen hours later, vancomycin level in blood drawn through the PermCath was 120 µg/mL. On the same day blood drawn by venipuncture showed vancomycin 10.1 µg/mL. Subsequently, vancomycin treatment was reinstituted with same dose of 1g/day. After one week of treatment, the trough vancomycin level was 10.2 µg/mL in blood drawn from a peripheral vein. The spurious toxic vancomycin concentration only in blood sampled through the PermCath is explained by vancomycin adhering to the line without affecting the systemic distribution of the drug.

The observation of spuriously high vancomycin level in blood sampled from a central venous line was confirmed by others [25]. There are reports of spurious plasma levels of other medications which were administered by venous line and blood sampled from the line to assess trough levels. This was the case for actinomycin-D [26], aminoglycoside [27-29] but not confirmed by others [30,31], ciclosporin [32] (not confirmed by others [30] and phenytoin [33]. The conflicting results were ascribed to different types of catheters in use having different degrees of molecule adhesions, or to variable sampling techniques [34-36]. At all, any aberrant result should be suspicious and should be verified by collecting blood from venipuncture.

Contamination of venous lines by microbiota

Bacterial contamination of venous lines is frequently observed. Indeed, about one third of blood cultures are false-positive by contamination [37,38]. Guidelines forward principles to prevent contamination of venous lines as well as rules for diagnosing catheter-related infection. These guidelines are widely known, so we mention only one basic principle when collecting blood for cultures in the febrile patient having a peripheral or central venous line. If the cause of fever is unknown, blood cultures should be taken both from the venous line and by direct vein puncture. On the other hand, when taking blood cultures in a patient having a known or highly probable cause of the fever, it is not recommended to take cultures from the venous line; cultures should be taken from peripheral veins in two separate puncture sites. In genuine bloodstream infection both specimens will be positive with the same organism. In case of contamination only one specimen will be positive [39-43].

Conclusion

Spurious test results in blood drawn from peripheral or central venous lines are a continuing problem. Optimally, blood samples from intravenous line are taken only once, on insertion. However, when a venous line is already in use for frequent intravenous administration of medications, the line is sometimes used also for blood sampling. This practice can be an acceptable alternative, providing bedside rules are respected. Flushing and locking of intravenous catheters are necessary to prevent occlusion. Therefore, before blood is drawn for analysis through the venous line, an appropriate fluid volume should be discarded from the line to prevent pollution of the sample. Removing the waist volume may avoid spurious test results, but not always so. Awareness of the unusual or improbable should raise a red flag warning when: a) the test result is out of clinical context, b) different from previous laboratory tests, c) when extreme high or extreme low values are reported. Any dubious test result should be double-checked in blood drawn by venipuncture. When the spurious nature of the test is recognized, the cause of the artifact should be exposed, and measures be taken to be avoided in the future. Adhering to correct practice in drawing blood for analysis may avoid spurious test results, misdiagnosis and harm.

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