Rodenticidal anticoagulant poisoning

Sir,

The recent case report published by Iglesias et al. on superwarfarin rodenticide poisoning includes some salient points of interest, and is also a cause of reflection on the relationship between emergency medicine and clinical toxicology[1].

Since more than 10 years ago, rodenticides containing heavy metals causing very serious poisoning, sometimes difficult to diagnose, have disappeared[2]. Coumarins now feature in almost all pesticides and biocides on the market, with increasing use of superwarfarins, with a very long elimination half-life of several weeks in some cases. The Spanish literature on this type of poisoning is almost nonexistent, so this publication from Hospital de Sabadell is welcome.

The purpose of the Clinical Note was to provide an update on the plan of action to follow in cases of poisoning by superwarfarin rodenticides, but we missed an explicit indication on monitoring these patients in the short and medium term, as if 48 hours without alterations in coagulation tests were sufficient to ensure that coagulopathy would not appear later. These cases may develop hemorrhagic diathesis 9 days or more after ingestion and outcome may sometimes be fatal[3], so outpatient treatment is generally recommended with oral phytonadione and weekly monitoring of prothrombin time, as Iglesias et al. mentioned.

Such situations are an example of the care activities in clinical toxicology units (CTU), including continuity of care for emergency department (ED) patients requiring control after acute poisoning, due to the risk of complications which may be neurological (carbon monoxide), renal (NSAIDs), digestive (caustics) or respiratory (irritant gases), to name a few[4]. This model of CTU may or may not have a clinical toxicologist, and may depend on the ED, but not necessarily, because some of its functions are not related to emergencies[5].

Screening tests for warfarin compounds are not available in clinical practice in our health care environment, nor are chromatographic techniques that allow plasma quantification of these compounds. Therefore, no direct diagnostic confirmations are made, while any research that would correlate clinical severity with toxic concentrations is not feasible, which would provide basic knowledge for future patients[6].

In the ED it may be risky to establish the prognosis of these patients based on some specific values of INR or prothrombin. We believe that in cases of anticoagulant ingestion, prudence should guide the conduct of care based on administration of at least one dose of activated charcoal (if recent), the antidotal use of phytonadione, blood transfusion, plasma or prothrombin complex in the event of hemorrhagic diathesis and ambulatory monitoring[7].

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Author's Response

Sir,

We have carefully read the letter by Santiago Nogué et al. regarding our recently published clinical note[1]. Referring to the issues raised, we would like to make some observations. First, we agree about the need for clinical toxicology units, but until they exist in Spain, for cost-effectiveness reasons, emergency physicians together with other specialists can provide continuous monitoring of these patients. Second, screening tests for superwarfarin are performed in Spain. Thanks to the collaboration of the National Institute of Toxicology and Forensic Sciences, Seville, and especially the director Dr. Mª Luisa Sánchez Soria, we have been able to confirm newly diagnosed poisoning by superwarfarin in patients served by our emergency department. Thirdly, we agree on the administration of a single dose of activated charcoal, but we believe that the treatment sequence presented is evidence-based. The administration of vitamin K is the mainstay of treatment, but the slowness in restoring adequate levels of coagulation makes it insufficient to control bleeding in the ED. The administration of prothrombin complex in these patients, despite being empirically justified, has little support in the literature. There is little evidence, with few patients, and prothrombin complex has been mainly used in patients with INR below 3,5, which is far from the situation of altered coagulation and severity usually present in superwarfarin poisoning[2]. Furthermore, fresh frozen plasma contains insufficient concentrations of factors II, VII, IX and X (especially IX) to reverse the effect of anticoagulant medication, so is not optimal treatment[3,4]. Also, it requires thawing time and is not without risk of communicable disease inoculation[5]. Standardized treatment is still lacking, therefore, and must be individualized according to the patient's clinical situation. After reviewing the literature, we collected the experiences reflected in published cases, and treatment should be individualized

for each patient according to the clinical situation.

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How should we treat chemical buns of the eye and skin?

Sir,

Recently, Marquez de Aracena has raised the issue of ocular chemical burns and their treatment in EMERGENCIAS[1]. His interesting paper provides the results of a study in which the classical medical treatment was combined with plasma rich in growth factors (PRGF), applied topically or subconjunctivally, and compared with a control group. Apparently, the best performance is obtained when using the PRGF, but the author does not mention three important limitations: first, the small number of patients in each group (n = 5); second, the heterogeneity in the ability of chemicals involved to cause lesions (ranging from detergents or solvents to caustic soda); and finally, the variability in initiating both classical treatment (30 to 60 min) and PRGF (between 1 and 24 hours).

The treatment of eye and skin lesions after contact with chemicals is controversial. Most authors consider that washing / irrigation with water, very early (first minute), intense (quantity) and prolonged in time, is the most efficient, economical and universally available measure. Its objectives are to dilute and wash out the chemical, remove any foreign bodies and, in some cases, normalize the pH of the anterior chamber of the eye. The immediacy of treatment is the most influential factor in effectiveness, so one cannot waste any time looking for a specific solution if one has water, saline or Ringer's lactate available[2,3]. When using solutions, the minimum quantity is 500-1000 ml for at least 15 min.

There are some exceptions to these treatments with water, such as metallic forms of sodium, lithium or potassium, and alkaline products used in industry and whose reaction with water can be very violent, so decontamination is performed with gauze and subsequently oil. For calcium hydroxide, contact with water makes quicklime (calcium oxide), which behaves as a very strong base, so one must always brush the skin before irrigating. And, on the other hand, pure magnesium powder, sulfur, strontium, titanium, uranium, yttrium, zirconium or zinc may ignite or explode on contact with water.

But apart from the water, there are other more specific neutralizing or diluting agents that have been used for chemical exposures. Thus, a solution of polyethylene glycol 400 in isopropyl alcohol has been experimentally shown to reduce skin damage and absorption of phenol, since it is not soluble in water[4]. Irrigation with hexafluorine for cutaneous or ocular exposure to hydrofluoric acid or with diphoterine (an amphoteric hypertonic aqueous solution, for other acids, alkalis, oxidizing or very irritating agents) has shown very rapid and higher neutralizing capacity than water and better outcomes for some patients, without side effects[5-9].

The availability of a specific physical area in the ED for decontamination of chemical products, eyewash, showers, more specific decontamination equipment and a protocol (standard operating plan), may contribute to immediate symptomatic improvement and reduced sequelae[10].

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Author's Response

Sir,

The application of hemoderivatives for tissue regeneration, and in particular, that of the ocular surface, has aroused great interest[1,2]. These include PRGF[3], whose effectiveness in chemical burns[4,5] has recently been described in this Journal[6]. In this regard, Nogué et al., by letter, require further information6 which is detailed below.

On the number of patients, I must add that the field study was carried out during 3 years by the same specialist, covering over 300 burns by chemicals, but we only included those who met the inclusion criteria: male, young adults (18-50 years), healthy, without ocular or general background, without infections (including HIV, hepatitis a and B), with less than 3 hours to specialized care, burns due to accidents at work caused by chemical agents, authorized treatment and informed consent and, above all, with the same anatomical lesions (both in size and location and depth). Of these, only 15 met all the requirements.

Regarding the "lesional" capacity of the chemicals involved, we know that severity depends on product concentration, exposure time and the pH of the solution. Thus, based on these variables, the same chemical agent can produce multiple lesions, which condition evolution. Hence the main classifications of chemicals causing eye burns are made on the basis of concentration, exposure time and Ph, regardless of the etiologic agent involved (Roper-Hall, Dua[7]). Therefore, to determine the effectiveness of a particular therapeutic treatment, it is much more objective to compare similar lesions with the same anatomical characteristics, with the complexity that entails. The study does not assess the best way to prevent damage by chemicals coming into contact with the ocular surface, but rather the effectiveness of a new treatment to cure existing lesions.

About the initiation of treatment, as previously stated, the study was conducted on established lesions in which treatment was immediately instituted in all patients along with PRGF application within 24 hours. However, no differences were observed in the results regarding the start time in the different groups.

We detected some errors in the units of time, in Table 1 of the reference article[6] describing the patients studied. Thus, the type of treatment (Trt) appears with "(minutes)" when in fact it should not appear at all; TH (time to first hospital cure) appears with "(hours)" which should be "(minutes)"; tPRFR appears with "(days)" when it should be "(hours)" and for TC (time to wound healing) there is nothing but "(days)" should appear there.

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Delay in seeking emergency care for acute coronary symptoms: 30 years later

Sir,

The delay in diagnosis and appropriate treatment after a possible acute coronary syndrome (ACS) event is still excessive, and 40% of patients still die before receiving help. We fully agree with Bolivar et al. on the misinformation about the most rapid and appropriate action, and especially in the differences observed between men and women[1].

We confirm their findings with data from 94 female ACS, collected from 590 consecutively admitted patients. Women showed higher mortality (25.5% versus 8.7%, p <0.001), especially in the elderly group (41.4% in 70-79 years and 36.3% in> 80 years) as a result greater delay in access and the high incidence of mechanical complications, severe arrhythmias, pump failure, right ventricular extension and cardiogenic shock[2,3]. In addition, in Table 1, we show the differences in the main parameters studied in another work – between ACS admitted in the first hour after the onset of symptoms (H1) and the rest (HR)[4]. In group H1 there were more male patients, younger, with typical pain, less ischemic history, better hemodynamics and functional class, more serious arrhythmias (obvious cause of out-of-hospital death) and higher percentage of fibrinolysis (although very low, given the limitations at that time, even without percutaneous intervention). In the H1 group there was lower average length of stay and mortality than in patients admitted beyond that time. So the decision to rapidly seek coronary support seemed not to be based on previous episodes or signs of severe dysfunction.

The complexity of the problem

Table 1. Differences in the main parameters studied

Parameter (%) (except for age)	H1	HR	p
Male sex	80.4	78.4	0.05
Mean ge (years)	61	63	0.05
Typical pain	63.0	55.6	0.001
History of ischemia	53.2	73.4	0.001
Anterior location	38.0	38.0	NS
Inferoposterior location	43.4	43.7	NS
Killip functional class I at admission	77.1	75.8	NS
Forrester hemodynamic Grade I at admission	63.0	46.2	0.001
Primary ventricular fibrillation	15.2	5.4	0.001
Complete atrioventricular block	9.7	8.5	0.05
Floating pulmonary artery catheter	15.2	14.0	0.05
Temporary pacemaker	16.3	9.9	0.001
Mechanical ventilation	7.6	4.1	0.001
Aortic counterpulsation	1.1	4.6	0.001
Fibrinolysis	29.3	18.4	0.001
Average length of stay in ICU (days)	3.9	4.3	0.05
ICU mortality	8.7	10.3	0.05

ICU: intensive care unit; H1: patients seen within 1 hour of the onset of symptoms; HR: other patients. NS: not significant.

is illustrated by the fact that these data were collected 30-34 years ago and published in 1988[2] and 1991[4], respectively. Patient perception and reflection that motivates seeking assistance, more than a quarter century later, is still inadequate. Coronary patients, whatever their initial presentation, do not usually describe or interpret their symptoms correctly nor do they associate them with possibly serious cardiac events. In women with older age, symptomatic diversity and higher prevalence of diabetes and metabolic syndrome as risk factors, the delay in their seeking help suggests dependence on their menfolk, work obligations (mainly domestic), care of others and being alone[1,2,4-7]. We agree on the great need to improve information about ACS, especially for patients at risk and family members, from primary care and prehospital emergency services.

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Resources and use of Spanish emergency medical systems: the situation in Andalusia

Sir,

We read with interest the 2 original articles by Martín Reyes et al.[1] and Arcos González et al.[2], where they perform a review of doctors and nurses in emergency medical systems (EMS) of Spain and a comparative study of the care activities of regional EMS, respectively. Both show data related to the region of Andalusia that require clarification.

The numbers of professionals and resources in general refer to those of the Public Company for Health Emergencies (EPES) of Andalusia. As indicated in methods, Andalusian data were extracted from the website, but that is not included in the list of references. In Andalusia, emergency assistance is provided by EPES units and those of the Andalusian Health Service (SAS in Spanish). Without these specifications, the reader is only given some of the data. This is similar to that reported by Ballesteros[3] which has already generated a letter clarifying the actual data situation[4]. That letter highlighted, for example, how a total of 133 units and 479 mobile medicalized transport emergency units belonging to SAS were left out. This distorts the realities of health care in our community. We do not know whether this limitation affects some of the other communities analyzed.

With respect to these services[2], we think that there are two underlying problems. The first derives from the previous point, with a numerator not clearly defined, so any estimate is made for the overall population still overestimates actual activity. In fact, the numbers do not coincide with those given in our activity report for 2009. Moreover, we would like to see a more thorough description of the methodology on the definitions of each care activity and the resources. In this regard, we think it would be advisable to follow a model similar to that employed by the Ministry in its report on the Resources and Activity of Emergency Services 112/061 for the year 2012[5], which describes in detail, by autonomous communities and provinces, and which provides specific definitions of types of staff and resources.

We agree with the authors in their interest in the issue and possible implications. It is very likely that a significant variability between EMS in different regions of Spain could have influence on the final results in the health of their patients, but we believe there must be prior methodological adjustment to address such an important debate.

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Authors' response

Sr. Editor:

Regarding the comments made by Olavarria et al, we wish to clarify the following issues:

1. In the titles and objectives of the cited articles, the scope of study is specified as emergency medical systems and emergency coordination centers. To contextualize the issue it should be remembered that the Ministry of Health's report on the resources and activities of the emergency services and the call numbers 112/061 states that "The National Health System has three organizational resources to meet the demands of urgent care: that provided by primary care, that coordinated through 112/061 calls for out-of-hospital emergencies, and hospital emergency departments". Well, we understand that attention of emergencies by units of the An-

dalusian Health Service called Critical Care and Emergency Units are part of the services provided by primary care.

In addition, as appears in the Functional Plan of Critical Care and Emergency Units of the Andalusian Health Service (http://www.juntadeandalucia. es/export/drupaljda/FondoPlan- FuncionalDCCU.pdf), among their functions there appears "attending emergencies in its area of coverage 24 hours a day, both in the unit and in the patient's home or place where the emergency occurs, initiating treatment and stabilizing the patient while awaiting the arrival of the Emergency System teams. "In its own document, then, the Andalusian Health Service differentiates between the care services that the two types of unit provide.

That is why, based on the definitions in these documents, we excluded from the study the units referred to in the letter. A similar situation also occurs in some other autonomous communities, with different names for these units (emergency department of primary care, continuing care points, etc.). And in these cases we excluded them from the study because they do not form a direct part of the emergency system, but rather other health structures. Clearly, the different forms of management and organization of emergency health care in Spain complicate its study, and precisely for this reason, our study was limited to emergency medical systems, excluding other health structures which can potentially respond to an emergency.

2. About the source of data on Andalusia, at the beginning of the investigation we contacted the Management of the Public Company for Health Emergencies and asked them to facilitate access to data for 2009. Given their initial lack of response and our insistence on the importance of them being the ones to directly provide data, to avoid mistakes in the investigation, the literal answer was, "you have at your disposal the annual reports of our company, at www.epes.e (click on publications), from the year 2001". They also offered to send us a report for 2008 if we could provide them with our mailing address, but the fact is that, after providing our postal address, the report was never received.

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Respiratory distress in a man on heparin therapy

Sir,

Heparin-induced thrombocytopenia (HIT) is an antibody-mediated complication that promotes thrombosis[1-3]. There are few reported cases of HIT as an acute systemic reaction[4-6].

We report the case of a 77 year-old man, former smoker, with a pacemaker, history of chronic obstructive pulmonary disease, chronic renal disease, essential thrombocytosis treated with hydroxyurea and a recent diagnosis of urothelial carcinoma. He attended the emergency department with dyspnea and was diagnosed with pulmonary embolism. Anticoagulation was initiated with a bolus of unfractionated heparin (UFH) and perfusion. At admission laboratory tests showed hemoglobin (Hb) 8.9 g / dl, platelets (Pq) 348.000/mm^3, leukocytes (L) and creatinine 3.310/mm^3 1.9 mg / dl. After seven days the UFH was replaced with low molecular weight heparin (LMWH), suspended 24 hours later due to hematuria. Hb 8.4 g / dl and Pq 196.000/mm3 were observed. Once the bleeding was resolved, a new intravenous bolus of UFH was administered. Minutes later, the patient developed sudden dyspnea and cardiopulmonary arrest (CPA) that was reversed. In the intensive care unit (ICU) Pq of 43.000/mm^3 were observed. Suspecting progression of thromboembolism, a new bolus of UFH was administered and the picture was repeated, with Pq of 23.000/mm^3. Suspecting systemic reaction to HIT, lepirudin was initiated and positive antibodies against platelet factor 4 (PF4) was confirmed. Five days later, without further incident, the patient had 193.000/mm3 Pq. However, he died on the 9th day in the context of pneumonia.

HIT occurs in 0.5-5% of patients treated with heparin[1]. The mechanism is based on the binding of heparin to PF4 and reaction of the complex with circulating immunoglobulin G, which perpetuates platelet activation and endothelial damage[3,7]. The existing heparin-like receptors in the endothelium represent a target for complex: microembolization and vasospasm may occur in the pulmonary circulation explaining the acute respiratory and systemic manifestations[4]. Diagnosis is based on clinical suspicion according to the "4T" system[8] (Table 1) and the determination of antiFP4 antibodies[1,3]. HIT is more frequent after exposure to UFH in patients undergoing surgery[1-3]. For basic blood disorders, diagnosis can be difficult and falling values of platelets (> 50%) should be prioritized and not the absolute number[9]. Treatment is based on the suspension of heparin and administration of alternative anticoagulants, mainly danaparoid, lepirudin or argatroban[10]. Antivitamin K should be avoided because of the risk of skin necrosis[7]. The clinical presentation of severe respiratory distress can be considered a systemic manifestation of HIT after early re-exposure to the drug.

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Table 1. 4T Scoring system for patients with suspected heparin-induced thrombocytopenia. Pretest probability according to score: high 6-8, intermediate 4-5 and 0-3 low

	2 points	1 point	0 points
Thrombocytopenia	Fall of 50% or peak, 20,000-100,000/mm^3	Fall of 30-50% or peak, 10,000-19,000/mm^3	Fall of <30% or peak, <10,000 mm^3
Time since heparin exposure	5-10 days, or <1 day if there has been exposure to heparin in the last 30 days	After 10 days, uncertain onset or <1 day with exposure during the previous 30-100 days.	< 1day without recent exposure to heparin
Thrombosis or other events	Proven thrombosis, cutaneous necrosis or ı acute systemic reaction to IV bolus	Progressive, recurrent or silent thrombosis; erythematous skin lesions	None
Other causes	Not apparent	Possible	Definite

Adapted from Warkentin et al.[8]. *Minimum value observed.

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Severe hyponatremia secondary to polydipsia involving of isotonic drinks in a man with schizophrenia

Sir,

Altered levels of consciousness in relation to severe hyponatremia secondary to potomania is a rare disorder, associated with significant morbidity and mortality.

A 41 year-old man with chronic schizophrenic psychosis was attended for low level of consciousness, with a Glasgow Coma Scale (GCS) score of 8. Capillary blood glucose was 220 mg / dl. We administered flumazenil 0.5 mg iv, naloxone 0.4 mg iv. Oxygen therapy was started with a fraction of inspired oxygen (FiO2) of 50%. Spontaneous breathing at 15 rpm was maintained and arterial oxygen saturation (O_2 Sat) was 99%. In the emergency department he developed impaired consciousness (GCS 6). He immediately developed self-limiting tonic seizures, after which he received endotracheal intubation and mechanical ventilation. He remained hemodynamically stable. Laboratory tests showed hyponatremia (111 mmol/L), calculated plasma osmolality of 227 mOsm/kg, lactate 2.52 mmol/L, hypokalemia (3.1 mmol/L), hypochloremia (79 mmol/L), hipouremia (9 mg/dl), hypophosphatemia (2.3 mg/dl), hypomagnesemia (1.3 mg/dl) and hypocalcemia (0.86 mmol/L). Urinary osmolality was 64.88 mOsm/kg. Cranial computed tomography showed no abnormalities. The family described his abundant and regular intake of liquid (10 liters isotonic drinks), with no increase in daily intake in the previous days. Infusion of normal saline 0.9% was initiated, and the patient had frank polyuria 600-1000 ml/h. At 3 hours he presented Na+119 mmol/L (glucose solution was then introduced). At 48 hours serum sodium (136 mmol/L) normalized as were the other electrolyte abnormalities. Following the withdrawal of sedation, he regained consciousness without neurological injury.

Psychiatric patients often have polydipsia or psychogenic polydipsia-hyponatremia, especially patients with schizophrenia (6.6% present both)[1]. Encephalopathy secondary to hyponatremia is a medical emergency, and mortality is 15%[2]. One must ensure that the plasma natremia (1 mmol / h) is increased in a controlled manner and initiate saline infusion. Corrections should be no greater than 10-12 mmol in the first 24 hours and 18-25 mmol in the first 48 hours, due to the risk of central pontine myelinolysis[3]. If the correction is larger, we recommend glucose 5% adjusted to diuretic rate. The use of desmopressin can be considered in refractory cases[4,5]. Although there are references to cases with excessive intake of hyponatraemic beverages - water and beer[6,7], there are no references to cases after intake of sports drinks[8].

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Acute coronary syndrome as a cardiovascular sing of carbon monoxide poisoning: A report of 2 cases

Sir,

Poisoning by carbon monoxide (CO) is associated with high rates of morbidity and mortality, and is the leading cause of poisoning death in the United States[1]. Signs and symptoms are diverse, which can mimic many diseases. Cardiovascular manifestations in CO poisoning are rare[2], but involve a vital diagnostic challenge due to the therapeutic and prognostic implications.

An elderly couple were taken to the emergency department with dizziness and malaise. Both were at home with a gas heater burning, so CO poisoning was suspected. The woman, aged 73, experienced nausea, dizziness, shortness of breath and oppressive non-radiating central chest pain. On physical examination, the patient had a heart rate of 95 bpm, respiratory rate of 18 rpm, arterial saturation of 98% and a mean arterial pressure of 85 mmHg. Carboxihemoglina (CO Hb) was 26.2%. Oxygen therapy was initiated at high flow. A 12-lead electrocardiogram showed ST segment elevation in the inferior wall; she underwent urgent coronary angiography. The right coronary artery showed complete occlusion, and a conventional stent and complete revascularization was introduced with good results. Troponin I in the ER was 9.19 ng / ml (normal value <0.2 ng / ml), with peak troponin of 157, 9 ng / ml.

Her husband, aged 80, had a history of hypertension, smoking and atrial fibrillation treated with acenocoumarol, showed clinical signs of dizziness and diffuse

malaise, without chest pain or dyspnea. Physical examination was unremarkable but showed elevated levels of CO-Hb (12.5%). A 12-lead ECG showed chronic AF without significant acute changes, and seried myocardial damage enzymes were analyzed. The initial troponin was 2.41 ng / ml, so he was moved to the coronary care unit with a diagnosis of acute coronary syndrome without ST elevation. Peak troponin was 21.5 ng / ml. Scheduled cardiac catheterization revealed complete occlusion of the circumflex artery. Two stents were successfully implanted. Both patients had favorable outcomes, due to early diagnosis of ischemic heart disease triggered by CO poisoning and correct treatment.

Hemoglobin has a 240-fold greater affinity for CO than for oxygen. This results in left shift of the Hb dissociation curve, decreasing oxygen delivery to the tissues, resulting in cellular hypoxia. In preclinical models, CO poisoning in dogs caused a global and relative subendocardial hypoperfusion. In a review of 230 patients with CO poisoning, evidence of myocardial damage was detected in 37% as determined by ECG changes or elevated markers of myocardial damage, but catheterization was performed in only 7 patients, in whom coronary artery occlusion was confirmed in only 3 of them[5]. Kales et al[6]. analyzed deaths from cardiac causes in a group of firefighters, and found that those who were engaged in firefighting had a higher risk for coronary disease. In our patients we observed that in the context of cellular hypoxia by CO poisoning, acute coronary syndromes with thrombosis may develop, and these are not easily detected based solely on electrocardiographic changes. In conclusion we emphasize the importance of performing a 12-lead ECG, and the serialization of enzymes of myocardial damage in all patients admitted to the emergency department with suspected CO poisoning.

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