

## Hemolytic Anemia as an Outcome of Occupational Exposure to Formalin: A Case Report

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### ABSTRACT

**Background:** Occupational exposure studies indicate that formaldehyde exposure causes temporary and consistent effects on industrial workers exposed to formalin.

**Case:** The case was a 36-year-old man who had developed intravascular hemolytic anemia caused by formalin after inhalation exposure. Formalin is a clear solution of 37% formaldehyde in water. The primary route of exposure to formaldehyde is inhalation. The case was presented with severe Coomb's negative hemolytic anemia with hemoglobinuria and was treated successfully with therapeutic red cell transfusion and exposure removal.

**Conclusion:** All employers must provide a safe and healthy workplace for prevention of harmful effects of formalin. Elimination of formalin from workplace, implementation of local and general ventilation, and using proper protective equipments are the most effective methods in the workplace.

**Keywords:** Formalin, Hemolytic Anemia, Occupational Exposure.

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### INTRODUCTION

The premature destruction of erythrocytes is called hemolysis. If the bone marrow activity cannot compensate for the erythrocyte loss, hemolysis leads to hemolytic anemia. The symptoms of patients vary and depend on whether the onset of hemolysis is acute or chronic and on the portion of erythrocytes that are destroyed (1).

There are many etiologies for premature erythrocyte destruction. Some of these etiologies including abnormal hemoglobins, erythrocyte enzymatic defects, immune destruction of erythrocytes, mechanical injury, hypersplenism, and conditions such as intrinsic membrane defects (2). Another reason for hemolytic anemia is exposure to chemical substances such as occupational exposure. Formaldehyde (HCHO) is one of the most important products of the

chemical industry. It is used in manufacturing resins, particle board, plywood, leather goods, paper, pharmaceuticals, and many other products. As such, occupational and residential forms of exposure to this chemical have become quite common. Formaldehyde is a gas at room temperature. Low concentrations of formaldehyde are found in the air primarily as a result of burning organic fuel such as wood, coal, gas, oil, gasoline, or diesel fuel. Formaldehyde is readily absorbed through the lungs and gastrointestinal tract and, to a much lower extent, the skin. Formaldehyde is highly water-soluble and is usually absorbed in the upper airways and nose. It routinely does not penetrate deep into the lungs (3). The permissible exposure limits (PELs) for formaldehyde in the workplace are 0.75 part per million (ppm) measured as an 8-hour time-weighted average (TWA). The short-term exposure limit (STEL) of 2 ppm

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is the maximum exposure allowed during a 15 minute period. Human knowledge on systemic formaldehyde intoxication is inadequate as only few cases of formalin ingestion have been reported. Formaldehyde is a toxic, colorless, flammable gas with a pungent and irritating odor that extremely irritates the upper airways (4).

Moreover, there have been cases of formalin penetrating the circulatory system in haemodialized patients, which was caused by contamination of haemodialyzers with formalin used earlier for disinfection. Two patients died due to respiratory disturbances and acute intravascular haemolysis (5). In still other similar cases, symptoms of anaphylactic shock and acute intravascular haemolysis developed and caused death (6). The study findings indicate that in patients undergoing haemodialysis with formalin-disinfected haemodialyzers, the anti-formaldehyde antibodies are formed; if bigger amounts of formalin get to the circulation, the antibodies may lead to anaphylactic shock (7). In the present study, we report a patient with repeated hemolytic anemia following occupational exposure to formaldehyde.

### CASE PRESENTATION

A 36-year-old male patient was referred to the Department of Occupational Medicine of Baharloo Hospital in 2008 in order to study the relationship between his four cases of hemolysis with occupational exposure.

The symptoms of his illness first appeared in 2003 for the first time. Patient's Symptoms on hospital admission during the hemolysis periods were palpitation, weakness, cold sweating, nausea, and anxiety. After being referred to a hospital, the patient was diagnosed with hemolysis. Consequently, he was hospitalized another three times after presenting the same symptoms.

Before 2003, neither the patient nor his family members had any history of

surgery or specific illnesses. The patient had been working as a crusher operator in a poultry food production plant for 16 years.

His job was preparing the crushed grains of food and also maintenance of the crusher. The food consisted of corn, soya, wheat, barley, sunflower seed, fish powder and additive substances (chlorpromazine, furazolidon, oxytetracycline, and vitamins). Disinfection of the equipments with formalin was added to his duties from January 2003. Disinfection operation was conducted two times a day and formalin and potassium permanganate were used for this purpose. The main material was formalin and permanganate was rarely used. There were not any other workers in the room during the disinfection processes and his working hours were 8 hours per day, 6 days per week.

While using 40% formalin for disinfecting the products twice a day for duration of 10 minutes each, the patient had exposure to formalin vapor through inhalation as well as the deposited formalin on equipments and corn. He complained about throat burn and eye burn during his working hours. Worker's complaints from throat and eye burn increased while performing the disinfection processes. It is important to note that he did not wear respiratory protective devices and air conditioning equipments were deficient in the workplace.

Formalin air concentration was measured in the beginning, middle, and the end of shift. The mean air level of formaldehyde was 2.5 ppm. The formalin air concentrations were 1.3, 3.8, and 2.4 ppm in the beginning, the middle, and the end of shift respectively. The air level of potassium permanganate was undetectable and the average cumulative dust exposure was under OSHA permissible exposure limit for total dust. The room size where formalin was used by the worker was  $7 \times 4 \times 3.5$  meters ( $98 \text{ m}^3$ ).

**Table 1.** The hemolytic episodes of the patients

Measurement	Mar 2003	Jun 2005	Oct 2007	Aug 2007	Normal Values
WBC	-	3200	2500	1500	3.5-10×10 <sup>3</sup>
Hb	8.5	8.9	9.3	5.1	12.1-15.2g/dl
Plt	-	91000	124000	48000	150-450×10 <sup>3</sup>
T.Bil	-	1.5	2.5	3.8	0.5-1.2mg/dl
D.Bil	-	0.3	0.6	0.4	0.1-0.6mg/dl
LDH	-	1140	1450	2320	90-180IU/L

The admitting laboratory data for the four times of hemolysis are provided in Table 1. Upon admission to the hospital, hematologic consultation was performed for the patient and blood transfusion was prescribed for him at the last hospitalization. After hospital discharge, he was away from work site up to 2 months and then returned to his work. Return to work happened in a situation that no change had been made to the work place.

Hepatitis A, B, and C virus antigens and antibodies were all negative. In addition, antinuclear antibodies, anti-DNA antibodies were also negative. The peripheral blood smear showed polychromatophilia, anisocytosis, and macrocytosis.

Osmotic fragility and glucose-6-phosphate dehydrogenase activity were appropriate to the reticulocyte count. Sucrose lysis and Ham's test were negative. Bone marrow biopsy indicated hypercellularity with giant myelocytes, myeloid series being relatively normal. However, numerous investigations failed to reveal a cause for hemolysis.

## DISCUSSION

Formalin is a disinfectant material which is used as a tissue fixative for preserving biologic specimens for histologic examination. Formalin is a hazardous solution, so workers must observe special precautions for storage and handling processes.

All workers should be trained about the adverse effects of this material. They should be informed that formalin must never be stored without warning labels,

and if there is any doubt about the type of material in the bottle, it should be discarded (8).

Long-term exposure to the low levels of formaldehyde may cause respiratory difficulty, eczema, and sensitization (9).

Formaldehyde and other disinfectants, including acetic acid, peracetic acid, and hydrogen peroxide can be noxious to RBCs and cause hemolysis (10). There are also reports of a secondary hemolysis in hemodialysis patients when formalin is used for disinfection of equipments.

The symptoms after the exposure to formalin include irritation of the eyes, nose, and throat, along with increased tearing. These symptoms occurs at air concentrations of about 0.4 - 3 part per million (ppm) (9).

There is a report of a case of swallowing formalin resulting in convulsions, dic, and hypovolemic shock (because of gastrointestinal bleeding). Formalin has also an oxidant effect on RBCs that causes acute intravascular hemolysis.

In summary, this study reported a case with intravascular hemolytic anemia resulting from occupational exposure to formalin. Considering the fact that other causes of hemolysis were ruled out, it can be concluded that the hemolysis of the patient was due to exposure to formalin. Hemolysis was not repeated again when exposure was discontinued.

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