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# Renal failure and occupational exposure to organic solvents: what work-up should be performed?

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## Abstract

The etiological work-up of a disease with an occupational component, such as renal failure associated with exposure to organic solvents, may include several complementary investigations. We discussed certain elements of the aetiological work-up in the light of a clinical case, particularly the individual and collective advantages and disadvantages of this work-up. Further investigations would not have provided the patient with any individual or collective benefit and were therefore not performed, while other investigations (environmental studies, screening of fellow workers) may provide collective rather than individual benefits, but must be decided by a multidisciplinary approach. A multidisciplinary study (general practitioner, nephrologist, occupational health physician and specialist in toxicology) is necessary to discuss the appropriate aetiological work-up, taking into account the individual and collective benefit-risk balance.

**Author Keywords** Occupational disease ; Kidney disease (Failure) ; (Organic)Solvent ; (Etiologic diagnosis)

## Introduction

The etiological work-up of chronic kidney disease with renal failure often includes a search for toxic causes, including environmental or occupational causes [1]. However, although many investigations are now frequently performed in patients as a result of recent progress, the individual and collective benefit-risk balance of the aetiological work-up must be carefully considered.

The advantages and disadvantages of complementary investigations and subsequent management will be discussed in the light of a case report concerning patient consulting an occupational health unit.

## Results/Case report

### Medical data

A 47-year-old man was referred by his occupational physician to our occupational medicine unit for an advice concerning occupational management following the discovery of advanced chronic renal failure (declared as occupational disease, fitness for work).

Laboratory tests performed in a context of deteriorating asthenia and recently discovered severe hypertension showed elevated serum creatinine of 285 mol.L<sup>-1</sup> and 248 mol.L<sup>-1</sup> when repeated 6 months later. Creatinine clearance was 26 ml.min<sup>-1</sup> and 28 ml.min<sup>-1</sup> 6 months later. Investigation of this renal failure did not reveal any urinary tract obstruction, nephrotic syndrome, or electrolyte abnormalities. Haemoglobin and serum calcium were at the lower limit of normal. The aetiological work-up did not reveal any significant cardiovascular disease. Ultrasound showed no obstruction and a small, regular right kidney with no signs of polycystic disease, no vascular abnormalities and no thrombosis on Doppler studies. He had no particular personal or family medical history, with no history of infection or any particular treatment. The haematological, immunological and metabolic assessment was normal. In view of the patient's occupation, an occupational cause was therefore considered.

### Occupational data

The patient had worked as a painting assistant in several companies since the age of 18 in Algeria and then in France for the last 7 years. In his current job, for the last 6 years, the patient prepares cars painting 5 days a week from 8:30 a.m. to 12:00 a.m. and from 1:30 p.m. to 5:00 p.m. Paint preparation is performed in a workshop without windows or mechanical ventilation. The two doors of the workshop open onto a courtyard, but are kept closed during working hours. The patient's personal protection equipment comprises gloves, overalls and FFP1 masks that he does not use. The kitchen where the patient eats his meals is situated in the same workshop. Safety data forms for the paints prepared by the patient indicate that he was concomitantly exposed to various organic solvents while occupying his current job (especially unsubstituted aliphatic hydrocarbons such as naphtha and higher benzene analogues) in proportions ranging from 0.1 to 80%. No heavy metals were found in the painting.

In practice, evaluation of the patient's exposure to organic solvents can be reasonably considered to be greater than 20 hours a week for 6 years, which corresponds to a high level of exposure to organic solvents. The patient's exposure to organic solvents during his previous jobs could not be determined, but was very likely.

### **Review of the literature**

A review of the literature confirms that some of these solvents have been incriminated in the development of renal failure with varying levels of evidence [2 –6 ], as some studies appear to link organic solvents with certain forms of glomerulonephritis (immunological mechanism), such as membranoproliferative glomerulonephritis and IgA glomerulonephritis [6 –9 ]. The odds ratios linking exposure to organic solvents with glomerulonephritis reported in the literature range between 2.8 to 8.9 with a probable dose-effect relationship between the degree of exposure and severity of the disease [3 ,4 ,6 ].

A number of arguments also indicate toxicity of organic solvents on proximal tubular cells causing necrosis via oxidative stress (experimental studies and studies on glue sniffers [1 ,10 ]. Several studies provide concordant results concerning the aggravating role of solvent-induced renal failure [1 ,10 ,11 ]. For example, a large cohort study demonstrated significant deterioration of membrane nephropathy towards end-stage renal disease due to exposure to organic solvents, especially toluene/xylene and gasoline, fuel, gas-oil [12 ].

### **Discussion**

Various investigations could be proposed in this case to elucidate the associations between exposure to organic solvents and renal failure.

General investigations have been ever made to exclude non-occupational causes of renal failure. A possible lead exposure before the 1980's could have been hypothesised, especially by releasing of lead ions from bones. Nevertheless, even though we could not exclude this aetiology, the haematological investigations were normal.

Kidney needle biopsy is theoretically essential to identify the site of the kidney lesion and was discussed in this case to eliminate a lesion with no known occupational cause. However, in view of the advanced degree of renal failure of our patient, biopsy would very probably have shown only nonspecific and inconclusive abnormalities attributed to the invasive nature of the technique.

Salivary gland histology was also envisaged to exclude amyloidosis, but the absence of renal hypertrophy made such a diagnosis unlikely and, in any case, no specific treatment is available for this disease.

Confirmation and quantification of occupational exposure were also considered in order to corroborate solvent exposure (metrological samples), but such investigations only provide confirmation of exposure when they are positive and do not provide any information about the link between exposure and the patient's disease (especially as the exposure responsible for the disease may date back many years). Furthermore, negative results of this type of metrological study do not exclude possible exposure (solvents not assayed, solvents not handled on the day of sampling, etc.). Consequently, in view of the possible direct link between exposure to organic solvents and renal failure, and the possibly essential nature of the disease (no aetiology demonstrated), the patient was given a medical certificate in support of an occupational disease. The advantage for the patient of exclusion of the role of exposure would be to allow him to continue his current occupation. Nevertheless, in view of the products handled and the available data concerning this type of occupation, the probability of exposure is relatively high with a low negative predictive value for metrology. It therefore appears reasonable to suspend the patient's job aptitude and request a change of job to slow the progression to dialysis or renal transplantation.

The possible collective benefit of further investigations needed however to be discussed after consulting several specialists, as precise quantification of the risk in the workshop by environmental (metrological) and laboratory measures of exposure or its effects, for example by screening other employees, could provide a benefit in terms of collective prevention. This would allow primary prevention of unexposed employees, but also earlier detection of any renal abnormalities (secondary prevention). The disadvantage of this type of approach is the economic risk for small financially fragile companies. Apart from providing better individual medical, social and financial cover, declaration of an occupational disease can also contribute to improvement of overall working conditions for other employees.

### **Conclusion**

This case report illustrates the importance of limiting certain invasive investigations that only provide a limited benefit to the patient. However, other investigations with a collective benefit can be considered. A multidisciplinary approach (general practitioner, nephrologist, occupational health physician and specialist in toxicology) is therefore necessary to discuss the most appropriate work-up, based on assessment of the individual and collective benefit-risk balance.

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