Stimulating Effect of Gold Trichloride on DNA Synthesis of Human Lymphoid Cells

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Abstract

The effect of gold trichloride on DNA synthesis of human thymocytes and peripheral blood lymphocytes was tested. A stimulation was obtained in both cell types with a concentration of 6–50 $\mu\text{g/ml}$. Gold trichloride may thus not be used in a lymphocyte transformation test for the diagnosis of contact allergy.

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Gold salts are potentially strong sensitizers in vivo as shown by the maximization test [6]. Most gold salts also seem to be irritant [2]; gold chloride can easily give a false-positive reaction in patch testing [4].

In vitro cultured peripheral blood lymphocytes have been shown to be inhibited in their mitogenic lectin- and antigen-induced DNA synthesis by sodium aurothiomalate and gold trichloride [1, 7]. On the other hand, Schöpf et al. [11] reported a specific in vitro stimulation of peripheral blood lymphocyte DNA synthesis in a patient with a positive epicutaneous reaction to gold trichloride, and Denman and Denman [3] got a positive lymphocyte transformation in patients with adverse effects after therapy with sodium aurothiomalate.

In previous investigations [8, 10], mercuric chloride, in contrast to cobalt chloride and potassium dichromate, was shown to stimulate the DNA synthesis in human thymocytes, thereby eliminating its use in the lymphocyte transformation test for detection of contact sensitivity. In the present investigation the potential stimulating effect of gold trichloride on DNA synthesis was tested in human thymocytes and peripheral blood lymphocytes.

Gold trichloride ($\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$; Fluka, Switzerland) was prepared to a final concentration in the cultures of 1.5–100 $\mu\text{g/ml}$. Thymocytes were obtained from children undergoing heart surgery and peripheral blood lymphocytes from healthy adult donors without gold allergy. The different lymphocytes were separated on Percoll (density 1.129 g/ml; Pharmacia, Uppsala, Sweden) gradients on the basis of buoyant density [5, 8, 9]. Thymocytes with characteristics of medullary cells (mitogenic lectin-reactive) and peripheral blood lymphocytes were then resuspended in culture medium RPMI 1640 with addition of L-glutamine (2 $\mu\text{mol/ml}$), streptomycin (100 $\mu\text{g/ml}$), penicillin (100 IU/ml) and 15% heat-inactivated human AB serum to a concentration of 2×10^6 cells/ml. The thymocytes were incubated for 3 days and the peripheral blood lymphocytes for 6 days, in 100- μl cul-

Table I. DNA synthesis stimulating effect of gold trichloride in thymocytes and peripheral blood lymphocytes

The effect of different concentrations ($\mu\text{g/ml}$ culture medium) of gold trichloride on the incorporation of tritiated thymidine in DNA of thymocytes and peripheral blood lymphocytes,

incubated for 3 and 6 days, respectively, was tested. The activity in lymphoid cells from 5 individuals is given as percentage of the control (mean $\pm$ SEM) and for the control also in cpm (mean $\pm$ SEM) (in parentheses). ND = Not done.

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tures, in a Linbro microtitration plate at 37 °C in an atmosphere of 5 % CO₂ in air. After a preincubation for 30 min, 20 μ l of the gold trichloride solution or 20 μ l of saline was added. 6 h before interrupting the cultures, 0.5 μ Ci of 3H-thymidine (5 Ci/mmol; Radio-chemical Centre, Amersham) in 10 μ l saline was added to each well. The cells were then collected on a Skatron multiple-cell collector using glass fiber filters. Incorporated radioactivity was determined by counting in a Packard liquid scintillation spectrometer. The cultures were performed in triplicate. An evident DNA synthesis stimulation was obtained in both lymphoid cell types with a gold trichloride concentration of 6–50 μ g/ml (table I) while the highest concentration, 100 μ g/ml, was inhibitory. The stimulation degree was of the same magnitude in the thymocytes and peripheral blood lymphocytes. This is in contrast to the findings with mercuric chloride [8] and might indicate another mechanism for the stimulation. However, this stimulation excludes the possibility to use a lymphocyte transformation test for the diagnosis of gold trichloride contact allergy.

References

- Cahill, R.N.P.: Effect of sodium aurothiomalate 'myocrisin' on DNA synthesis in phytohaemagglutinin-stimulated cultures of sheep lymphocytes. *Experientia* 27: 913–914(1971).
- Cronin, E.: Contact dermatitis, p. 334 (Churchill Livingstone, Edinburgh 1980).
- Denman, E.J.; Denman, A.M.: The lymphocyte transformation test and gold hypersensitivity. *Ann. rheum. Dis.* 27: 582–589 (1968).
- Fregert, S.; Kollander, M.; Poulsen, J.: Allergic contact stomatitis from gold dentures. *Contact Dermatitis* 5: 63–64 (1979).
- Goust, J.M.; Perry, L.R., Jr.: Separation of human thymocytes at different stages of maturation by centrifugation on a discontinuous gradient of colloidal silica gel. *Thymus* 3: 25–33 (1981).
- Kligman, A.M.: The identification of contact allergens by human assay. III. The maximization test: a procedure for screening and rating contact sensitizers. *J. invest. Derm.* 47: 393–409 (1966).
- Lipsky, P.E.; Ziff, M.: Inhibition of antigen- and mitogen-induced human lymphocyte proliferation by gold compounds. *J. clin. Invest.* 59: 455–466(1977).
- Nordlind, K.; Henze, A.: Stimulating effect of mercuric chloride and nickel sulfate on DNA synthesis of thymocytes and peripheral blood lymphocytes in children. *Int. Archs Allergy appl. Immun.* 73: 162–165(1984).
- Nordlind, K.: Fractionation of human thymocytes and peripheral blood lymphocytes on Percoll density gradients and DNA synthesis stimulating effect of mercuric chloride. *Int. Archs Allergy appl. Immun.* 75: 16–19(1984).
- Nordlind, K.; Henze, A.: Investigation of ability of the metal allergens cobalt chloride, nickel sulfate and potassium dichromate to give a mitogenic response in human thymocytes. *Int. Archs Allergy appl. Immun.* 75: 330–332(1984).
- Schöpf, E.; Wex, O.; Schulz, K.H.: Allergische Kontaktstomatitis mit spezifischer Lymphocytenstimulation durch Gold. *Haut-arzt* 27: 422–424(1970).