This procedure for measuring aggregate represents a modification of methods as described.^{1,2} To my knowledge there is no method one can use to obtain pure aggregate. The classical method for obtaining aggregate employing centrifugation in caesium chloride density gradients does not yield 100% aggregate. There are nonaggregatable proteoglycans present in this fraction as well.

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References

- 1 Hardingham T E. Proteoglycans from bovine nasal cartilage: properties of a soluble form of link protein. *Biochem J* 1979; **177**: 237-47.
- 2 Tang L H, Rosenberg L, Reiner A, Poole A R. The role of link-protein in the structure of cartilage proteoglycan aggregates. *J Biol Chem* 1979; **254**: 10523-31.

Chromosomes in rheumatoid arthritis

SIR, Lymphoproliferative disorders are more frequently found in patients with autoimmune disease than in normal persons. Isomaki *et al*¹ showed an increased risk of leukaemia, lymphoma, Hodgkin's disease, and multiple myeloma in rheumatoid arthritis (RA) patients. These investigators postulated that a continuous immunological stimulation in RA could cause proliferation and malignant transformation of the immunologically competent cell clones. Green *et al*.² believe that immunodeficiency in patients with autoimmune disease may be a factor in the development of lymphoproliferative disease.

We found marked chromosomal abnormalities in a patient with lymphoma who was treated with intra-articular radioactive gold (¹⁹⁸Au) for severe RA.³ Although we were tempted to conclude the chromosomal abnormalities found in our patient were due to her ¹⁹⁸Au treatment, we were unable to exclude the possibility that the phenylbutazone and prednisone treatments or the development of her lymphoma or RA may have been the cause of the chromosomal abnormalities. This communication reports our chromosomal findings of 21 RA patients with various treatments and of 28 controls.

Heparinised peripheral blood was obtained for cytogenetic studies from 21 active RA patients. Five patients received 10 mCi of intra-articular ¹⁹⁸Au; 14 received intramuscular nonradioactive gold; and 2 received full therapeutic doses of aspirin (7800 mg/day). The controls consisted of 28 hospital employees without any known illnesses. Peripheral blood was cultured in TC 199 tissue culture medium, enriched with either autologous plasma or fetal calf serum and stimulated with phytohemagglutinin (PHA) according to the method used in our laboratory.³ After incubation at 37°C for three days the cultures were exposed to colcemid at a concentration of

0.16 µg/ml for one hour. The cells were then exposed to 0.075 M KC1 for half an hour, fixed with acetoalcohol, and the slides made by the air-dried method. The slides were stained with Giemsa and analysed for chromosomal breakages as described.⁴

The mean rate of chromosomal breakages was 8.6 ± 2.4 (SEM) in the 5 RA patients treated with ¹⁹⁸Au; 9.4 ± 1.43 in the 14 treated with nonradioactive gold; and 5.5 in the 2 treated with high doses of aspirin. The 28 controls had a frequency of 3.67 ± 0.56. The mean difference of the chromosomal breakages among the RA patients, treated with radioactive or nonradioactive gold, was not statistically significant. But the difference between the RA patients and the controls was significant.

Acquired chromosomal abnormalities can be seen in patients exposed to radiation, virus, and certain chemicals or in patients with various malignant diseases. The marked chromosomal abnormalities found and reported³ in our patients with lymphoma, treated with ¹⁹⁸Au for her RA, must not have been caused by the radioactivity of the ¹⁹⁸Au per se. This conclusion is based on our present finding that significant chromosomal breakages are also seen in RA patients treated with nonradioactive gold. Although it is possible that the chromosomal abnormalities found in our RA patients were associated with their primary disease rather than their treatment, we cannot make this conclusion based on our present data, since all our patients were treated with various methods. Also, it is not possible to study RA patients not treated with aspirin to rule out this possibility.

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References

- 1 Isomaki H, Hakulinen T, Joutsenlahti U. Lymphoma and rheumatoid arthritis. *Lancet* 1979; **i**: 392.
- 2 Green J A, Dawson A A, Walker W. Systemic lupus erythematosus and lymphoma. *Lancet* 1978; **ii**: 753-6.
- 3 Goh K O, Jacox R F, Anderson F W. Chromosomal abnormalities: findings in a patient with lymphoma and rheumatoid arthritis treated with intra-articular gold Au-198. *Arch Pathol Lab Med* 1980; **104**: 473-5.
- 4 Goh K O. Total-body irradiation and human chromosomes. IV. Cytogenetic follow-up studies 8 and 10½ years after total-body irradiation. *Radiat Res* 1975; **62**: 364-73.

Klebsiella, ankylosing spondylitis, and statistics

SIR, Eastmond *et al*.¹ have followed up by post 44 ankylosing spondylitis patients. They obtained monthly a questionnaire about the clinical activity of the disease and a faecal specimen for klebsiella culture. They state that 18 patients on 19 occasions had *K. aerogenes* cultured from