

pathway of memory and naive CD4<sup>+</sup> cells [6], and the capacity of the CD4<sup>+</sup>CD45RO subset to concentrate in the inflammation area [7] or to infiltrate subcutaneous metastases of human melanoma [8], further emphasise, in accordance with our results, the involvement of CD4<sup>+</sup> T cells during *in vivo* IL-2 administration and their increased recirculation, in particular for the memory subset. Conversely, CD56<sup>+</sup>CD3<sup>−</sup> natural killer (NK) cells, after a slight and not significant decrease in the percentage 24 h after starting the IL-2 infusion, show a marked increase, peaking on the last day of the cycle. Even 2 days after stopping the infusion NK cells remain at a value higher than the baseline. It is also interesting to note the slight increase of circulating lymphocytes bearing the CD69 surface antigen, a molecule described as being acquired early after activation of T lymphocytes and NK cells [9, 10]. While the increase of the CD4<sup>+</sup> and CD8<sup>+</sup> T-lymphocyte subsets bearing the CD69 antigen is very slight and peaks the last day of the infusion cycle, the CD69<sup>+</sup> NK cells increase early and markedly, peaking after 24 h of rIL-2 infusion (Fig. 1). The expression of this molecule precedes the expression of other activation molecules such as IL-2R and DR [10], suggesting an early involvement of circulating NK cells and of a smaller percentage of T-lymphocytes during *in vivo* rIL-2 administration.

In conclusion, our results strengthen previous observations of the involvement of NK cells and CD4<sup>+</sup> T-lymphocytes, in particular with memory phenotype, in the immune modulation induced in cancer patients treated with systemic IL-2, and the role of this lymphokine in regulating lymphocyte recirculation.

*Eur J Cancer*, Vol. 29A, No. 3, p. 475, 1993.  
Printed in Great Britain  
0964-1947/93 \$6.00 + 0.00  
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## The Contribution of the Aminopyrine-breath-test in Metastatic Liver Disease

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THE 14C-aminopyrine-breath-test (BTA) is a well established functional liver test [1]. Surprisingly, there are no data in the literature reporting the use of the test in metastatic liver disease.

We here report our preliminary results, on the prognostic value of 14C-BTA in metastatic disease.

The test was performed after an overnight fast in the classical manner [1]. In 14 normal subjects [8 males, 6 females; average age mean (S.D.) 50 (13.5) years] the excretion rate was 5.2 (1.28)%. Patients with cancer but without liver metastases before or after chemotherapy showed a mean result of 4.4 (1.3)% [20 males, 14 females; average age 44 (16) years].

Patients without cancer, but with proven diffuse liver disease (5 males and 2 females; average age 56 (12) years) showed marked reduction [1.66 (0.66) %] and 14 patients with cancer without liver metastases but with known non-malignant hepatic disease [14 cases; 9 males, 5 females; average age 49 (8) years] also showed abnormal BTA values [1.9 (0.8)%].

19 patients with proven liver metastases were tested prior to chemotherapy. Of these 1 had a solitary metastasis, 15 multiple metastases and 3 had diffuse liver involvement. 3 patients with multiple metastases and all 3 with diffuse liver involvement had an abnormal (lower than 3%) BTA value. Of these 6 cases biochemical liver tests were only slightly disturbed (lowered PTT) in 4 patients. Nevertheless 4 patients died rapidly with advancing disease and signs of hepatic failure.

Of 24 patients with liver metastases who received several courses of chemotherapy, 9 had abnormal BTA values (lower than 2.5%). In 6/9 cases conventional liver function tests were only slightly perturbed. Nevertheless the patients with low BTA values died rapidly with terminal hepatic failure and abnormal echographic and/or computed tomography findings.

In conclusion, in patients with liver metastases, a significantly lowered 14C-BTA value, either before, during or after chemotherapy, is a prognostic index even if concurrent biochemical liver tests are normal or only slightly disturbed.

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Received 16 Apr. 1992; accepted 29 June 1992.