Metabolites of arachidonic acid in activating platelets and their estimation by radionuclide techniques

To the Editor: In their paper "Metabolites of arachidonic acid in activating (better: "activated") platelets and their estimation by radionuclide techniques" in the Hellenic Journal of Nuclear Medicine 2006; 9(1): 49. T. Daskalou and co-authors are reviewing the arachidonic acid pathway and its metabolites and in particular oxidation injury [1].

In contrast to the abstract, the isoprostane 8-epi-PGF_{2a}, the most relevant and reliable measure of in-vivo oxidation injury, is not even touched. This is a pity as 8-epi-PGF_{2a} is a relatively robust parameter which probably as the only one so far found its place in today's clinical routine in a variety of conditions.

In contrast, determination of classical metabolites of arachidonic acid, such as PGI_2, thromboxane (TX) A_2 and even PGE2 failed to contribute significantly to clinical routine, mainly due to methodological difficulties in sampling and processing. The authors are reporting physiological levels for PGI_2 and TX, definitely by orders of magnitude being too high. PGI_2, a natural antiaggregatory compound, for example, is only locally found and immediately metabolized to its stable (hydrolysis) derivative 6-oxo-PGF_{1a}. Its plasma levels are considered to range below 1 pg/ml. This range has been confirmed by GC-MS-determination [2]. Values at the range given (194.2±41.5 pg/ml) definitely reflect either sampling (activation) or processing or storage (cross reaction due to (per-)oxidation and subsequent isoprostane formation?) artefacts. The same holds true for TXA2 which is determined in plasma via its stable (hydrolysis) derivative TXB_2 or even better its metabolite in parenchymal organs, 11-dehydro-TXB_2 [3]. The most reliable parameter, however, is 2,3-dinor-TXB_2 measurement in urine. It's really difficult if not impossible to draw blood absolutely avoiding platelet activation. Only a few destroyed platelets may double TX-values measured. This, directly or indirectly via cross reactivity, may contribute to the (more than one order of magnitude too) high "normal" levels of "TXA_2" reported which should read TXB_2. If determined by GC-MS, TXB_2-values definitely range below 5 pg/ml too. A similar methodological problem exists for PGE2 with a plasma half-life of less than 1 minute being rapidly metabolized to 15-keto-13,14-dihydro-PGE_2 [4] which again rapidly undergoes subsequent chemical reaction in blood. Values for PGE_2 in plasma are ranging around 5 mg/ml. There is a world-wide consensus achieved almost 2 decades ago that the bicyclo-E metabolite is the most reliable parameter to determine. The trick behind is that incubating at pH 10-11, all PGE_2-metabolites are converted into the bicyclo-compound, which is then measured. Besides artificial and sampling artefacts in-vitro formation during storage and processing [5] are causing an artificial increase and are limiting factors for clinical application too. Definitely the only one prostaglandin parameter which can be recommended today for routine use being robust and informative in diagnosis and therapeutic monitoring or prognostic evaluation is the isoprostane 8-epi-PGF_{2a}, its values in plasma in (healthy non-smoking people without cardiovascular risk factors) men normally ranging below 20 pg/ml.

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Authors' reply:

In reply to the comments of Prof. H. Sinzinger referring to our paper under the title "Metabolites of arachidonic acid in activating platelets and their estimation by radionuclide techniques", in Hell J Nucl Med 2006; 9: 49-52, I would like to mention the following: a) It is true that isoprostane 8-Iso-Prostaglandin F_{2a}, 8-iso-PGF2a and 8-epi-PGF_{2a} (old name according to Former) or more correctly $15F_{2t}$-isoprostane 15-F2t-IsoP (new name according to Taber) is the most reliable biochemical–endocrinological index of lipid peroxidation in many abnormal conditions [1]. Normal values to IsoP were not mentioned in our paper because the test was performed by enzymoimmunoassay and not by radioimmunoassay which would be more familiar to nuclear medicine physicians. Normal values are 46.9±5.7 pg/ml, analogous to normal values of others [2,3] and almost identical to what we found in a recent paper of ours [4]. b) Normal values of thromboxane A2 as mentioned in our article, refer to the stable metabolite TXB_2 as is correctly mentioned by Prof. H. Sinzinger. The plasma levels of the stable metabolite TXA_2, that is the TXB_2 as mentioned in our article, are analogous with those mentioned by others [5,6] and in a recent article of ours [7]. Additionally, we note that we have preferred to measure plasma TXB_2 and not urine 11-dehydro-TXB_2 because we were measuring in parallel this biomolecule in patients on chronic heamodialysis where urine collection is a problem per se. We take every technical precaution for the accuracy of our results (indomethacine inhibitor etc). Also, small differences in normal plasma levels of TXB_2 may be due to dietetic and environmental factors [8,9]. c) Normal values of prostacycline I_2 as mentioned in our article refer to its stable metabolite, the 6-keto-PGI_2 as is correctly mentioned by Prof. H. Sinzinger. Normal values of this stable metabolite mentioned in our article are similar to those of others [10]. Small differences are due to dietetic and environmental factors [11]. d) Normal values of PGE_2 as mentioned in our article being 6.1±1.2 pg/ml are analogous to normal values of others [12]. Please notice that these plasma values are expressed in pg/ml and not in mg/ml as mentioned by Prof. H. Sinzinger.

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Our experience from radioiodine-131 treatment and whole body scintigraphy findings in 357 patients with metastatic differentiated thyroid carcinoma after surgical ablation

To the Editor: We consider of interest our experience on the above subject as follows: From September 1991 to October 2005, in the Departments of Nuclear Medicine: in Ostrava, Czech Republic and in Martin, Slovak Republic, we have studied 357 patients with differentiated thyroid cancer (DTC), 70 men and 287 women, with a mean age of 48.4 y. Sixty-six patients had follicular cancer (18%), 214 papillary cancer (60%) and 77 a mixed follicular and papillary type of cancer (22%). From the 357 patients, 231 had one surgical thyroid ablation, 106 had two and 20 had three surgical ablations before. These patients were treated by iodine-131 (^{131}I) after thyroid hormone treatment was withdrawn. Thyroid remnants were ablated with 3.7 GBq of ^{131}I. Five days or 6-12 months after ^{131}I treatment, a whole body scan (WBS) was performed. In the second case 300 MBq of ^{131}I were administered. A hundred and thirteen patients were examined by WBS. A double headed single photon emission tomography (SPET) camera (Siemens ECAM, Germany) equipped with high-energy collimators was used for scanning. In 96 patients diagnostic WBS was negative (Table 1). Patients with a positive WBS were retreated by a standard dose of 7.4 GBq ^{131}I. Treatment by thyroid hormones followed.

Thyroid stimulating hormone (TSH), free thyroxine (FT4), total triiodothyronine (TT3), thyroglobulin (Tg) and antithyroglobulin antibodies (TgAb) were tested in all patients. One patient was treated twelve times. The interest of our presentation lies on the following: a) By the WBS metastases in the kidneys, brain or skin were not detected [1]. b) In accord with our experience, favourable response to treatment was characterised by a parallel decrease of the tumour volume, the ^{131}I uptake and serum Tg levels [2]. c) Preparing patients for radioiodine treatment we did not use recombinant human TSH for administrative and financial reasons [3]. d) Patients may take up to 66.6- 88,8 GBq of ^{131}I within a 10 y period of time [4]. e) After one to twelve radioiodine treatment doses, the WBS in 85 percent of the patients was negative while normalization of Tg levels indicated successful ^{131}I treatment [5]. This is a randomised study. Selected patients will be studied and presented in a forthcoming occasion.

Table 1. *Number of ^{131}I treatments and whole body scan findings in our patients*

No of ^{131}I treatments with 7.4 GBq	No of patients	Post ^{131}I treatment WBS		
		negative	positive	localization of metastasis
1st	68	67	1	lung
2nd	23	17	6	lymph node, lung, liver
3rd	2	–	2	bone, lung
4th	1	–	1	thyroid remnant
5th	8	4	4	lymph node, lung
6th	1	–	1	lung
7th	1	–	1	liver
8th	4	4	–	–
9th	4	4	–	–
12th	1	–	1	lymph node
Total	113	96 (85%)	17(15%)	–

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