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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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A FLAVOUR OF DEATH: PERINDOPRIL INDUCED THICK MELANOMA AND BCC OF THE BACK. POTENTIAL ROLE OF THE GENERIC SUBSTANCE OR/-AND POSSIBLE NITROSAMINE CONTAMINATION AS SKIN CANCER KEY TRIGGERING FACTORS

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Abstract.

Contamination of certain drugs and foods with one of the most potent carcinogens/mutagens- nitrosamines, remains to be an issue and unresolved at present. The increased contamination of these mutagens in the most commonly used drugs in the human population doesn't ceases to baffle clinicians, critics, public scholars, and analysts of the nitrosamine saga.

The introduction of permissive determinations of the presence of carcinogens in drugs only reinforces doubts about the powerlessness of regulatory authorities in the face of the influence of powerful pharmaceutical cartels.

The FDA's encouraging promises of 2018 for strict control of carcinogens in sartans seems to have been permanently forgotten?

By 2021, it was unthinkable that these carcinogens would be present in blood drugs and affected batches were immediately removed. Following alert checks confirming their post-existence in diabetes drugs, anti-smoking drugs, a number of antibiotics, ACE inhibitors, Sartans, thiazide diuretics, ranitidine, but probably a number of others, the decision has been taken to give the green light to their permissible availability. An availability that in all likelihood has the flavour of death. A ″flavour″ that has been confirmed in hundreds of international publications. Or in data from scientific papers submitted to regulatory regional units for verification and which remain sadly silent to this day. The ″silent confirmation″ and the lack of any adequate response in favour of public health are a sufficient further indicator of the attitude and position of the regulatory authorities. A position that should be changed.

Starting from the mentioned facts and the data announced already in 2016/2017 of all-American data shared originally in American scientific journals, using their statistical estimates, we present the first case in the world literature of nodular melanoma and basal cell carcinoma occurring after taking perindopril. This intake turns out to be confirmatory one with respect to the statistics presented by Beatrice Nardone dating back to 2017. The potential pro-carcinogenic effects of both nitrosamines and the generic substance of perindopril are discussed.

Key words. Perindopril, generic substance, nitrosamine contamination, skin cancer, melanoma, BCC.

Introduction.

Contamination of heterogeneous drugs with nitrosamines appears to be a serious, currently ubiquitous, and unfortunately still ″unsolvable″ problem [1]. According to the official bulletins of pharmaceutical giants such as Pfizer, for example, this contamination affects ACE inhibitors as well as hydrochlorothiazide diuretics [2]. Pfizer has in fact turned out to be the only company to confront and publicly air the problem that concerns the health of millions (if not billions) of patients, while at the same time withdrawing all its contaminated preparations from the market [2]. Unfortunately, this gesture of loyalty/prevention aimed at patients was not adopted by the majority of pharmaceutical companies distributing nitrosamine-contaminated batches of drugs.

Notwithstanding this issue, the vigilance of clinicians regarding the aforementioned dilemma (presence or absence of contamination) , was sharpened and directed in a particular direction- namely : that of monitoring and registration of side effects following the intake of contaminated and non-contaminated drugs.

Thus, in practice, on the basis of negative clinical results, one could come to the solution of problems concerning global health and the cause of the cancer pandemic in general: the problems defining the puzzle of carcinogenesis.

We report the first reported case of a patient taking the ACE inhibitor perindopril who developed two skin tumors simultaneously: nodular melanoma of the medial inner part of the left thigh and basal cell carcinoma of the back. The potential role of nitrosamines (as a possible contaminant) , as well as of the generic substance in relation to the development of skin cancer is discussed.

Case report.

An 80-year-old male with a 5-year-old history of an arterial hypertension came to the dermatology department for a primary consultation and second opinion.

Since 2018 the patient was on systemic therapy with perindopril arginine/indapamide 5 /1,25 mg -half a tablet once in the morning, bisoprolol fumarate 2.5 mg once in the morning and clopidogrel 75 mg once in the morning. After 2,5-3 years from starting the initial therapy (2018), the patient noticed changes in the shape, texture and color of a small lesion located on the right inner thigh area. According to the anamnestic data, in the beginning the lesion was small in size, pigmented and wasn't "distinguishable" from the other moles located on the body. The duration of the presence of the pigment lesion is about 5-6 years before the initiation of therapy for arterial hypertension. Otherwise, the patient denies food and drug allergies; reports no history of painful sunburns nor malignancy in any family member.

In 2020 radiotherapy was conducted up to 12x4 Gy on the occasion of a slowly growing lesion on the back, 2 cm in diameter, cytologically verified as a basal cell carcinoma.

Other comorbidities were reported as follows: appendectomy, steatosis of the liver, cholelithiasis, prostatic hyperplasia and ischemic heart disease. The patient was stented twice in 2012 and 2014.

The dermatological examination showed a dark black-brown pigmented tumor formation with uneven texture and crusts located on the right inner thigh region (Figure 1a-e). Above the tumor formation a reddish discoloration with uneven borders can be noticed. Multiple telangiectasias and lentigo solaris can also be seen on the surrounding skin.

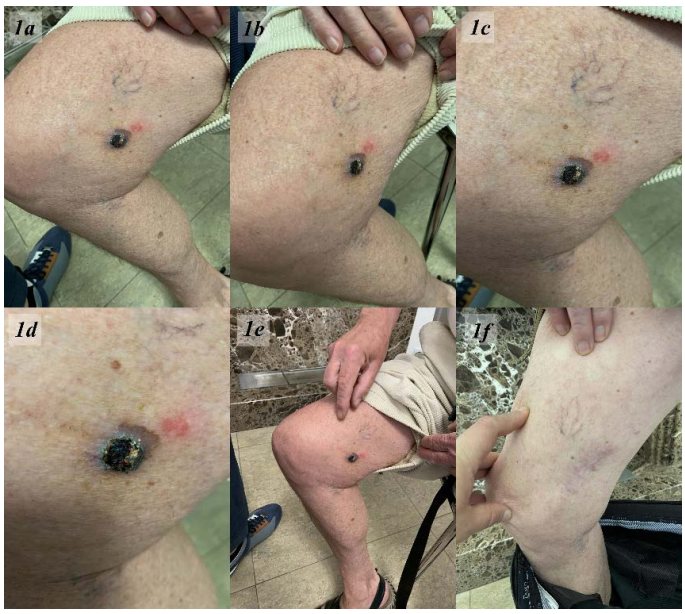

Figure 1. 1a-e: *Dark black-brown pigmented tumor formation with uneven texture and crusts located on the right inner thigh region.* ***1f:*** *A cicatricial lesion after the melanoma excision.*

The lesion was surgically removed in 2021 in an oncosurgical department with an initial surgical safety margin of 2cm. The histological result showed a nodular malignant melanoma with a diameter of 15 mm, Breslow tumor thickness 4.2 mm, Clark level 4, with ulceration, mitoses 6 mm/sq, vertical growth, moderate amount of melanin pigment and scarce lymphocytic stromal reaction, BRAF negative, staged pT4bN0M0. Detection and removal of sentinel lymph node has not been performed.

Postoperatively performed PET/CT scan showed a single hypermetabolic mesenteric lymph node located at L3 level, highly suspicious for melanoma metastasis. Pulmonary micronodules, inconclusive of malignancy, were found and were also subject for further follow-up. The patient was reevaluated at stage pT4b cN0 cM1a malignant melanoma. Initial ten courses of immunotherapy with pembrolizumab were started.

In 02.12.2022 another PET/CT scan was performed which resulted in positively therapeutically affected mesenteric lymph node and lack of dynamics of the previously described pulmonary micronodules. Small lymph nodes with reactive nature in the right hilus were noticed. A newly appeared small metabolically active focus on the skin of the left lower leg was seen, which was referred for a follow-up and dermatological control. The immunotherapy was continued.

A change in the antihypertensive therapy with perindopril was also recommended.

Discussion.

The first literature data showing a link or association between the intake of ACE inhibitors and the development of melanocytic and keratinocytic tumors dates back to 2017, when the nitrosamine issue was still completely unknown [3].

These data are fully suggestive regarding the risk of developing basal cell carcinomas, squamous cell carcinomas and melanomas after taking ACE inhibitors [3]:

1) For BCC: Adjusted (95% CI) OR **2,23** (1,78-2,81)/ unadjusted (95% CI) OR **2,09** (1,87-2,34)

2) For melanoma: Adjusted (95% CI) OR **1,71** (0,97-3,00)/ unadjusted (95% CI) OR **2,42** (2,00-2,95).

3) For SCC: Adjusted (95% CI) OR **1,94** (1,37-2,76)/ unadjusted (95% CI) OR **2,53** (2,07-3,08).

The conclusion that could be drawn from the data presented by Nardone B et al. [3] is that, in practice, the risk of developing the 3 most common forms of skin cancer is about or approximately doubled after taking ACE inhibitors [3]. It remains an open question whether the active ingredient (or so-called generic drug- substance) could in fact also be the cause of these ″higher rates of association″?

Or could it be due to the presence of so-called nitrosamines- known contaminants and mutagens found in the three classes of drugs: ACE inhibitors, sartans and thiazide diuretics?

Additionally, it is clear from colleagues' data that intake of all three classes of drugs: ACE inhibitors, sartans, and thiazide diuretics, could be associated with the development of all three forms of skin cancer: basal cell, cutaneous melanoma, and squamous cell carcinomas [3].

Despite the existence of a number of data, conditioning the high current mortality and morbidity (in terms of not only heterogeneous cancers in patients/ not in animals or in experimental settings) of patients after contact with nitrosamines (like inhalation for example) [4,5], the claim of the controlling/ regulatory authorities that ″these nitrosamines″ do not pose a danger to humans sounds like another sinister grotesque. Perhaps it is also because they do not pose a danger to humans that these preparations are being withdrawn from the market - quickly and quietly?

However, the data presented by Nardone B et al. [3] provide a very logical explanation why our patient developed two forms of skin cancer simultaneously after taking perindopril- nodular melanoma and basal cell carcinoma: it is unlikely that the mechanism of action of ACE inhibitors affects carcinogenesis concerning both keratinocytic forms of cancer and melanoma.

Surprisingly, analogous to completely overlapping/identical data are also available concerning the administration of sartans/ sartans in combination with hydrochlorothiazide (potentially contaminated with nitrosamines), after which the concomitant development of basal cell carcinomas and dysplastic nevi is again observed [6,7].

The development of multiple verrucous carcinomas and giant acral melanoma in the calcaneal region during therapy with potentially contaminated olmesartan and valsartan further supports the hypothesis of the possible presence of an independent, common carcinogen-or so-called nitrosamine [8].

On the basis of expert opinion from teams working extensively on this issue, it could be assumed that the presence of nitrosamines in any or all preparations would probably also lead to the development and progression of heterogeneous forms of skin cancer [9]. But not only.

Last but not least, interesting data should be mentioned regarding the role of the generic substance in ACE inhibitors, which is able to stimulate the aggressive behaviour of already present melanoma cells under experimental conditions [10].

Similarly, the observation described by other author teams in experimental conditions that sartans could potentiate metastasis in already present melanoma cells [11].

Unanswered but also somewhat rhetorical questions then remain:

1) Do nitrosamines generate heterogeneous cancers such as melanomas and basal cell carcinomas ? Answer : An undeniable fact at present, at least from a clinical point of view !

2) Do the generics in ACE inhibitors and sartans potentiate the progression of cancers that have already arisen: such as melanoma for example ? Answer: Similar to the previous question- there are strong clinical observations in this regard as well.

The simultaneous generation of nodular melanoma and basal cell carcinoma in the patient we described, as well as the subsequent metastasis of melanoma within the continued administration of ramipril, can only support this thesis of a definite, significant reciprocity between the experimental data and the clinical observations in the case presented .

A ″Case″ that should also be indicative of the role of personalized medicine and its impact on public health. The therapist's compulsory awareness should regain its significance by becoming his or her main, leading , and only moral priority.

Conclusion.

The overlapping patterns of clinical manifestation or development of heterogeneous forms of skin cancer after administration of completely different drugs in their mechanism of action, again supports the presumption of the presence of possible common carcinogens of human relevance and ubiquitous distribution, which is poorly controlled and out of regulation. Although these carcinogens have already been identified and half-officialized by the FDA and EMA.

The legalization of the permissive availability of carcinogens from EMA -without it simultaneously (as of now) being disclosed even in the package insert of the contents of a particular drug, remains to satiate one of the greatest absurdities in the history of medicine: for lobbying and protectionism in favor of pharmaceutical companies. Companies who have been allowed over the last 20-30 years to distribute batches of medicines contaminated with carcinogens as impunity. Medical products ″carrying the flavour of death″.

The identification of these carcinogens, their cataloguing and the subsequent mandatory mutational analysis of the tumors newly arising within their intake, should be the top priority of the drug regulators and pharmaceutical companies : complete elimination/banning, not formalization and initialing of permissible availability.

Ignoring these steps and recommendations would lead to the continuation and worsening of the cancer pandemic, or the business for billions: business to the detriment of global health and business in absolute defiance of Hippocrates' postulates.

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