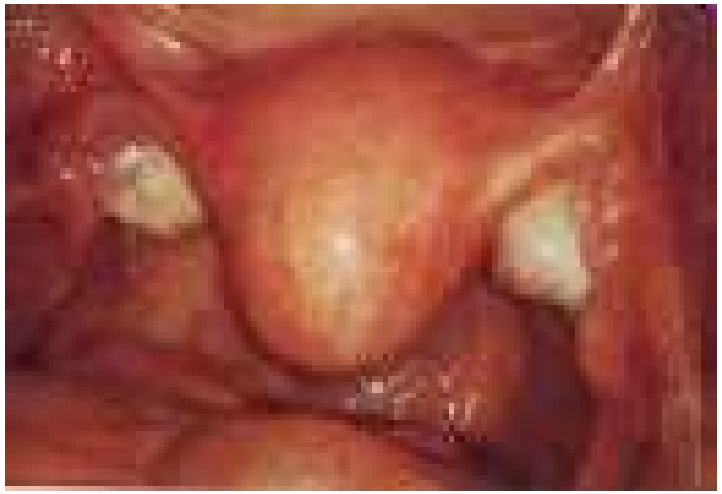


Fibroids are the most common indication for hysterectomy in the United States; a total of 300,000 hysterectomies to remove fibroids are performed each year. The overall cost of treating fibroids was estimated at $2.1 billion in 2000.[7] More than 70% of those costs were directly related to hysterectomy.

Hysterectomy and risk of stress-urinary-incontinence surgery: nationwide cohort study

Daniel Altman, Fredrik Granath, Sven Cnattingius, Christian Falconer

Summary

Background Hysterectomy for benign indications has been associated with an increased risk for lower-urinary-tract sequela, but results have been inconclusive. We aimed to establish the risk for stress-urinary-incontinence surgery after hysterectomy for benign indications.

INTERPRETATION: Hysterectomy for benign indications, irrespective of surgical technique, increases the risk for subsequent stress-urinary-incontinence surgery. Women should be counselled on associated risks related to hysterectomy, and other treatment options should be considered before surgery.

World J Urol
DOI 10.1007/s00345-010-0585-8

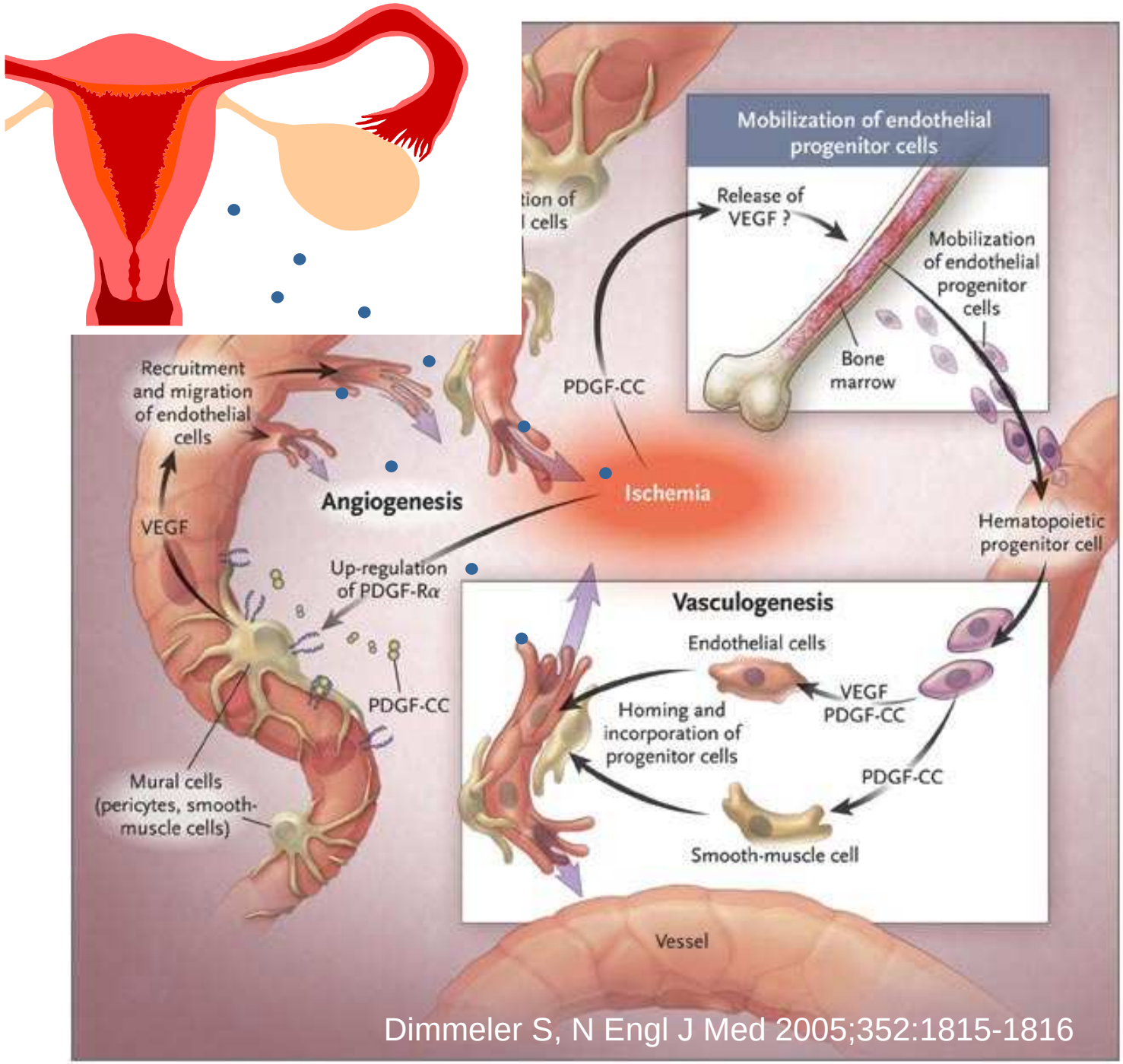
ORIGINAL ARTICLE

Genetic susceptibility to urinary incontinence: implication of polymorphisms of androgen and oestrogen pathways

J. N. Cornu · B. Merlet · O. Cussenot · G. Cancel-Tassin · C. Ciofu · G. Amarenco · F. Haab

Received: 3 January 2010 / Accepted: 5 July 2010

… AR polymorphism (combination of 2 alleles containing more than 21 CAG repeats) is significantly associated with UUI (P = 0.02). Polymorphisms of ESR-1, CYP17 and CYP19 were not associated with any subtype of urinary incontinence. …



Dimmeler S, N Engl J Med 2005;352:1815-1816

Increased risk of thyroid cancer among women with hysterectomies

Riitta Luoto, MD,[a] Seija Grenman, MD,[b] Salla Salonen, StudMed,[b] and Eero Pukkala, PhD[c]

Tampere, Turku, and Helsinki, Finland

OBJECTIVE: Hysterectomy with bilateral oophorectomy has been suggested to increase the risk of thyroid cancer. We studied the relationship between hysterectomy and thyroid cancer in a population-based setting in Finland.

STUDY DESIGN: Women undergoing hysterectomy between 1986 and 1995 (n = 17,900) were identified from the National Hospital Discharge Registry. The cohort was followed up through the Finnish Cancer Registry until 1997.

RESULTS: There were 118 cases of thyroid cancer diagnosed, 103 papillary and 15 follicular or medullar type. The incidence for thyroid cancer was significantly elevated (standardized incidence ratio [SIR] 1.38, 95% CI 1.15-1.64). The increase in the incidence of thyroid cancer was not dependent on the extent of operation but on the length of follow-up. Thyroid cancer incidence was increased 0.5 to 1.4 years after hysterectomy (SIR 2.00, 95% CI 1.31-2.93), but decreased thereafter (SIR 1.30, 95% CI 0.99-1.67). Hysterectomy with and without oophorectomy was associated with a similar increase in the incidence of thyroid cancer.

CONCLUSION: Women who have undergone hysterectomy have an increased risk of thyroid cancer during the first 2 years after the operation. Thyroid cancer and bleeding disorders may share a common background. (Am J Obstet Gynecol 2003;188:45-8.)

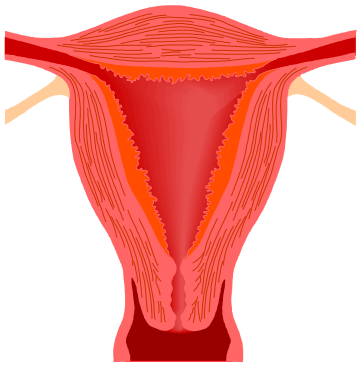
0013-7227/03/$15.00/0
Printed in U.S.A.

Endocrinology 144(10):4250–4252

doi: 10.1210/en.2003-0848

Modulation of Uterine Iodothyronine Deiodinases—A Critical Event for Fetal Development?

The outer ring deiodination of T_4 leads to the production of T_3, which is considered the active thyroid hormone that interacts with nuclear receptors and regulates gene transcription (1–3). T_3 outer ring deiodination (ORD) also generates another biologically active metabolite, the 3,5-diiodothyronine that exerts important metabolic effects, as described recently (4). Therefore, the ORD is considered an activating thyroid hormone metabolic pathway. Iodothyronine deiodinases are classified into three isoenzymes, based on several biochemical criteria and on different protein serum and intracellular T_3 levels during fetal development have to be regulated to be maintained in a narrow range, depending on tissue demands. During embryogenesis, thyroid hormone receptors are expressed and occupied before the onset of fetal thyroid function, showing that an important maternal-fetus thyroid hormone transfer occurs early in gestation (17). Nevertheless, there is a marked gradient of T_4 from the mother to the fetus and circulating T_4 and T_3 are lower in the fetus, probably due to the fact that during development D3 is the predominant enzyme expressed in most



Carvalho DP, Endocrinology, 2003;144(10):4250-4252.

0013-7227/03/$15.00/0
Printed in U.S.A.

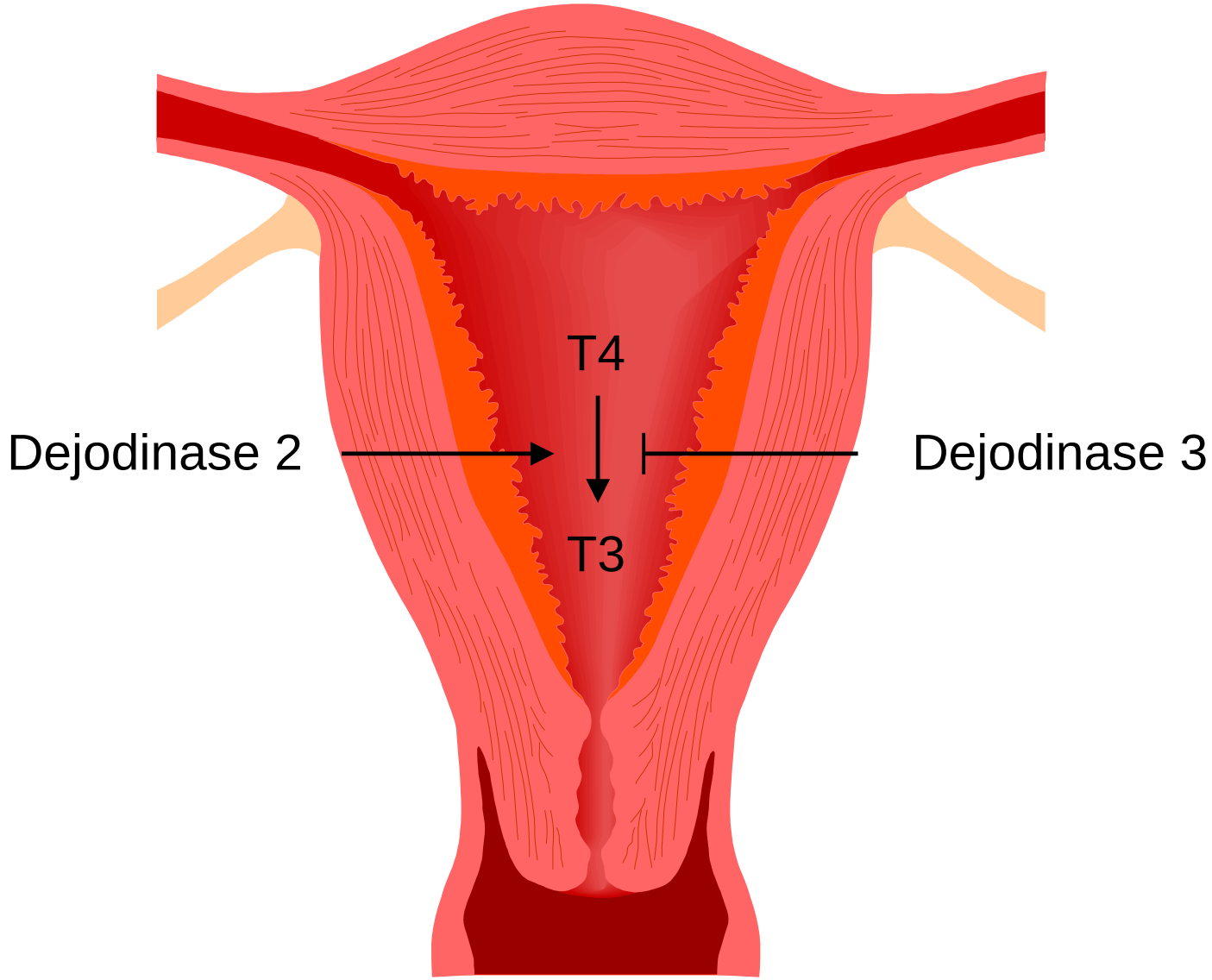
The Journal of Clinical Endocrinology & Metabolism 88(3):1384–1388

doi: 10.1210/jc.2002-021291

Type 3 Iodothyronine Deiodinase Is Highly Expressed in the Human Uteroplacental Unit and in Fetal Epithelium

STEPHEN A. HUANG, DAVID M. DORFMAN, DAVID R. GENEST, DOMENICO SALVATORE, AND P. REED LARSEN

Division of Endocrinology, Diabetes, and Hypertension (S.A.H., P.R.L.) and Department of Pathology (D.M.D., D.R.G.), Brigham and Women's Hospital, Boston, Massachusetts 02115; Division of Endocrinology (S.A.H.), Children's Hospital Boston, Boston, Massachusetts 02115; and Dipartimento di Endocrinologia ed Oncologia Molecolare e Clinica, Universita'degli Studi di Napoli "Federico II" (D.S.), 80138 Naples, Italy



Carvalho DP, Endocrinology, 2003;144(10):4250-4252.

Efficacy and tolerability of CDB-2914 treatment for symptomatic uterine fibroids: a randomized, double-blind, placebo-controlled, phase IIb study

Lynnette K. Nieman, M.D.,[a] *Wendy Blocker, R.N.,*[a] *Tonja Nansel, Ph.D.,*[b] *Sheila Mahoney, M.S., C.N.M., M.P.H.,*[a] *James Reynolds, M.D.,*[c] *Diana Blithe, Ph.D.,*[d] *Robert Wesley, Ph.D.,*[e] *and Alicia Armstrong, M.D.*[a]

[a] Program in Reproductive and Adult Endocrinology, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; [b] Division of Epidemiology, Statistics and Population Research, National Institute of Child Health and Human Development; [c] Department of Radiology, The Mark O. Hatfield Clinical Research Center; [d] Contraception and Reproductive Health Branch, National Institute of Child Health and Human Development; and [e] Biostatistics and Clinical Epidemiology Service, Warren Grant Magnuson Clinical Center, National Institutes of Health, Bethesda, Maryland

Objective: To evaluate the efficacy and tolerability of the P receptor modulator CDB-2914 (Ulipristal, CDB).

Design: Randomized, placebo-controlled double-blind clinical trial.

Setting: Clinical research center.

Patient(s): Premenopausal women with symptomatic uterine fibroids.

Intervention(s): Once-daily oral CDB (10 or 20 mg) or placebo (PLC) for 12 weeks (treatment 1). A second 3-month treatment with CDB (treatment 2) was offered. A computer-generated blocked randomization was used.

Main Outcome Measure(s): Magnetic resonance imaging (MRI)-determined total fibroid volume (TFV) change was the primary outcome; amenorrhea and quality of life (QOL) were secondary end points.

Result(s): Treatment 1 TFV increased 7% in the PLC group, but decreased 17% and 24% in the CDB10 and CDB20 groups. The TFV decreased further in treatment 2 (–11%). Amenorrhea occurred in 20/26 women taking CDB and none on PLC. Ovulation resumed after CDB. Hemoglobin improved only with CDB (11.9 ± 1.5 to 12.9 ± 1.0 g/dL) as did the Fibroid QOL Questionnaire symptom severity, energy/mood, and concern subscores, and overall QOL scores. The CDB was well tolerated, with no serious adverse events. Adverse events were unchanged during treatments.

Conclusion(s): Administration of CDB-2914 for 3–6 months controls bleeding, reduces fibroid size, and improves QOL. (Fertil Steril® 2011;95:767–72. ©2011 by American Society for Reproductive Medicine.)

Key Words: Selective progestin receptor modulator, ulipristal acetate, fibroids, UFS-QOL

0163-769X/05/$20.00/0
Printed in U.S.A.

Endocrine Reviews 26(3):423–438

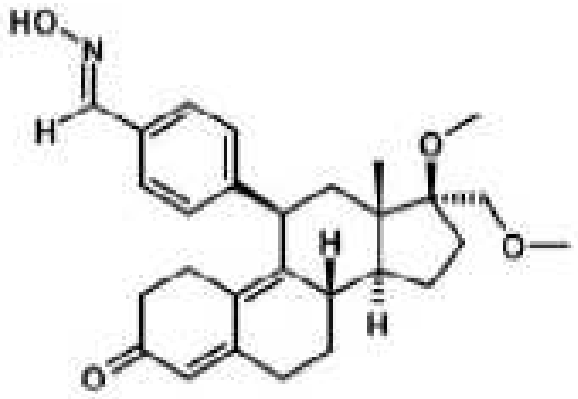
doi: 10.1210/er.2005-0001

Selective Progesterone Receptor Modulator Development and Use in the Treatment of Leiomyomata and Endometriosis

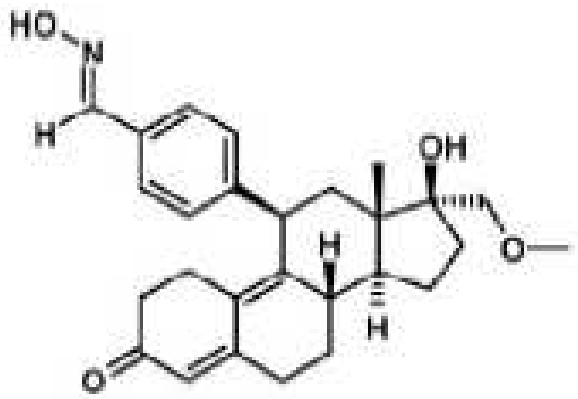
Kristof Chwalisz, Maria Claudia Perez, Deborah DeManno, Craig Winkel, Gerd Schubert, and Walter Elger

TAP Pharmaceutical Products, Inc. (K.C., M.C.P., D.D.), Lake Forest, Illinois 60045; School of Nursing (C.W.), Georgetown University, Washington, D.C. 20007; Jenapharm GmbH & Co. (G.S.), 07745 Jena, Germany; and EnTec GmbH (W.E.), 07745 Jena, Germany

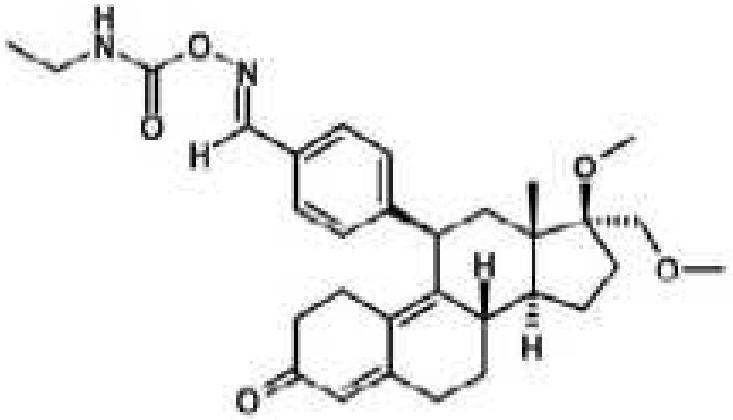
Selective progesterone receptor modulators (SPRMs) represent a new class of progesterone receptor ligands. SPRMs exert clinically relevant tissue-selective progesterone agonist, antagonist, or mixed agonist/antagonist effects on various progesterone target tissues *in vivo*. Asoprisnil (J867) is the first SPRM to reach an advanced stage of clinical development for the treatment of symptomatic uterine fibroids and endometriosis. Asoprisnil belongs to the class of 11β-benzaldoxime-substituted estratrienes that exhibit partial progesterone agonist/antagonist effects with high progesterone receptor specificity in animals and humans. Asoprisnil has no antiglucocorticoid activity in humans at therapeutic doses. It exhibits endometrial antiproliferative effects on the endometrium and breast in primates. Unlike progesterone antagonists, asoprisnil does not induce labor in relevant models of pregnancy and parturition. It induces amenorrhea primarily by targeting the endometrium. In human subjects with uterine fibroids, asoprisnil suppressed both the duration and intensity of uterine bleeding in a dose-dependent manner and reduced tumor volume in the absence of estrogen deprivation. In subjects with endometriosis, asoprisnil was effective in reducing nonmenstrual pain and dysmenorrhea. Asoprisnil may, therefore, provide a novel, tissue-selective approach to control endometriosis-related pain. SPRMs have the potential to become a novel treatment of uterine fibroids and endometriosis. (*Endocrine Reviews* 26: 423–438, 2005)



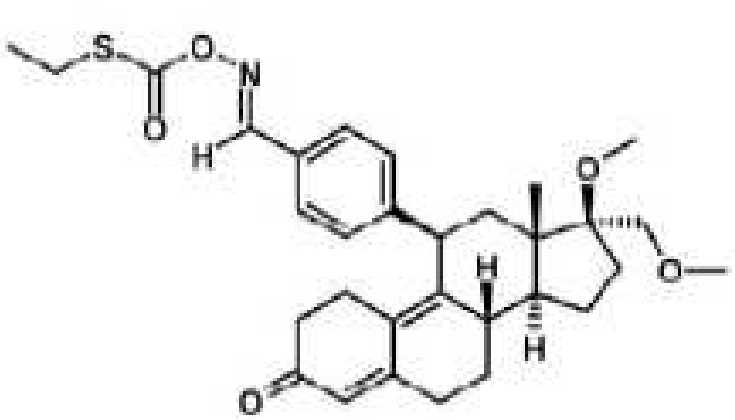
J 867 (Asoprisnil)



J 912



J 956 (Asoprisnil ecamate)



J 1042

A randomized, controlled trial of asoprisnil, a novel selective progesterone receptor modulator, in women with uterine leiomyomata

Kristof Chwalisz, M.D., Ph.D.,[a] *Lois Larsen, Ph.D.,*[a] *Cynthia Mattia-Goldberg, M.S.,*[a] *Anthony Edmonds, M.S.,*[a] *Walter Elger, M.D., Ph.D.,*[b] *and Craig A. Winkel, M.D., M.B.A.*[a]

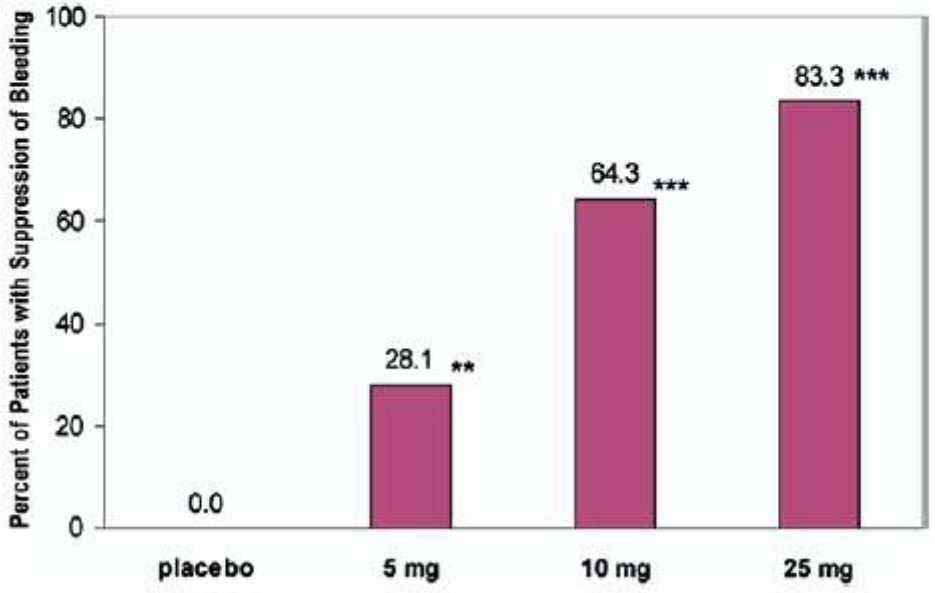
[a] TAP Pharmaceutical Products Inc., Lake Forest, Illinois; and [b] EnTec GmbH, Jena, Germany

Objective: To determine efficacy and safety of asoprisnil in patients with leiomyomata.
Design: Phase 2, multicenter, prospective, randomized, double-blind, placebo-controlled, parallel-group study.
Setting: Twenty-eight sites in the United States and 1 in Canada.
Patient(s): One hundred twenty-nine women with leiomyomata.
Intervention(s): Asoprisnil (5, 10, or 25 mg) or placebo orally daily for 12 weeks.
Main Outcome Measure(s): Uterine bleeding changes by using daily bleeding diaries, hemoglobin concentrations, dominant leiomyoma and uterus volume measured sonographically, patient-reported symptoms related to bloating and pelvic pressure, endometrial thickness and morphology, hormonal parameters, and standard safety measures.
Result(s): Asoprisnil suppressed uterine bleeding in 28%, 64%, and 83% of subjects at 5, 10, and 25 mg, respectively, and reduced leiomyoma and uterine volumes. Median percentage decrease from baseline in leiomyoma volume was statistically significant at 25 mg compared with placebo after 4 and 8 weeks of treatment; by week 12, leiomyoma volume was reduced by 36%. There was a significant reduction in bloating with the two highest doses and in pelvic pressure with 25 mg by week 12. Asoprisnil was associated with follicular-phase estrogen concentration and minimal hypoestrogenic symptoms.
Conclusion(s): After 12-week treatment, asoprisnil controlled uterine bleeding while reducing leiomyoma volume and the associated pressure symptoms. Asoprisnil was well tolerated. (Fertil Steril® 2007;87:1399–412. ©2007 by American Society for Reproductive Medicine.)

Key Words: Amenorrhea, asoprisnil (J867), leiomyoma, pelvic pressure, selective progesterone receptor modulators (SPRMs), menorrhagia, progesterone receptor, endometrium

FIGURE 2

Suppression of uterine bleeding during treatment with asoprisnil. Suppression of uterine bleeding was defined as having no light, medium, and heavy bleeding from the end of baseline menses through the end of dosing. $^{**}P \leq .01$ and $^{***}P \leq .001$ compared with placebo, by using Fisher's exact test.



Chwalisz. Treatment of leiomyomata with asoprisnil. Fertil Steril 2007.

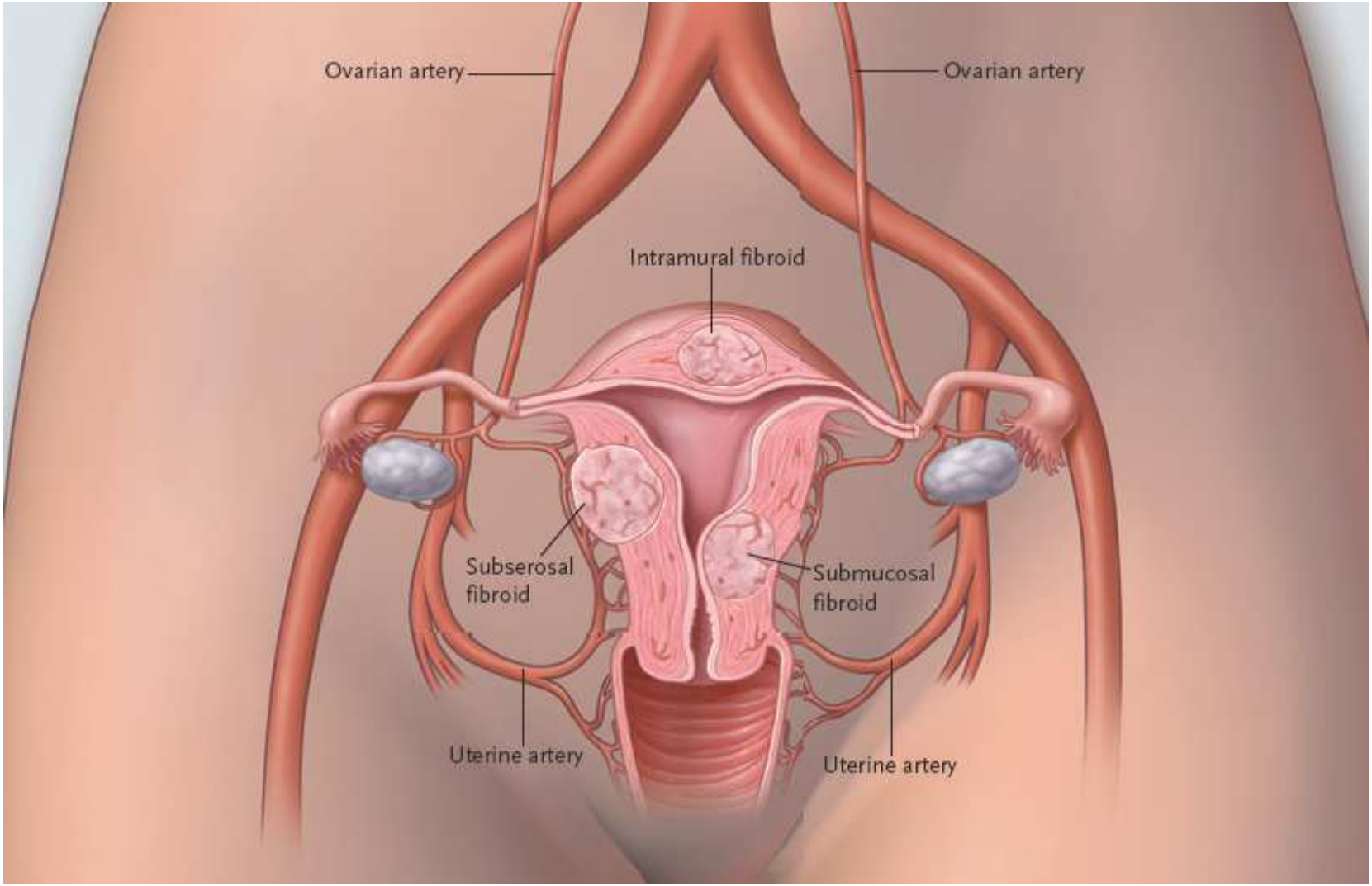
The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL THERAPEUTICS

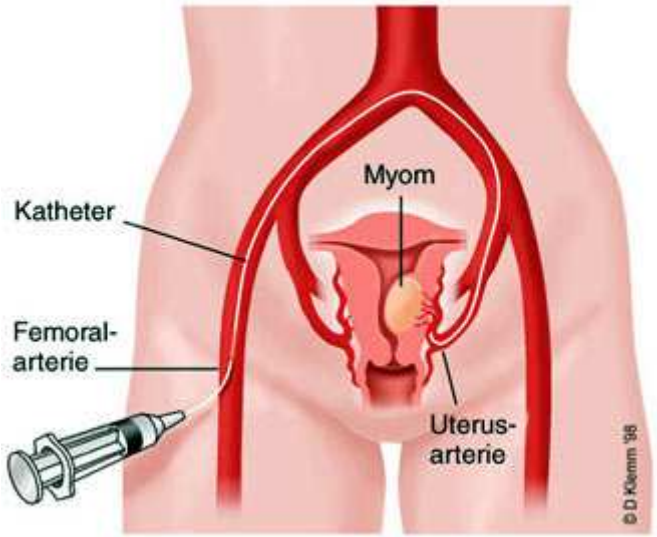
Uterine Fibroid Embolization

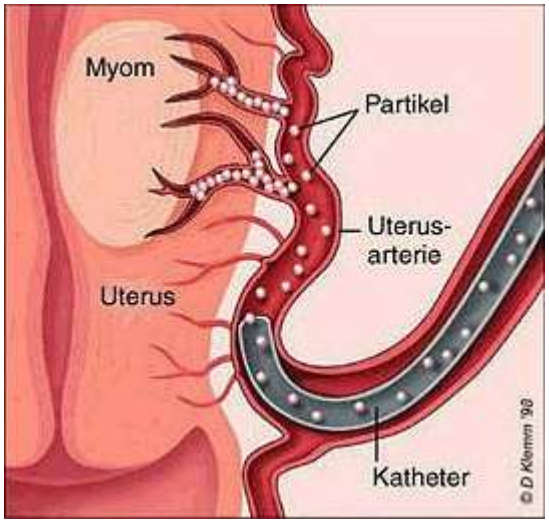
Scott C. Goodwin, M.D., and James B. Spies, M.D., M.P.H.

This Journal *feature begins with a case vignette that includes a therapeutic recommendation. A discussion of the clinical problem and the mechanism of benefit of this form of therapy follows. Major clinical studies, the clinical use of this therapy, and potential adverse effects are reviewed. Relevant formal guidelines, if they exist, are presented. The article ends with the authors' clinical recommendations.*


Ovarian artery
Ovarian artery
Intramural fibroid
Subserosal fibroid
Submucosal fibroid
Uterine artery
Uterine artery

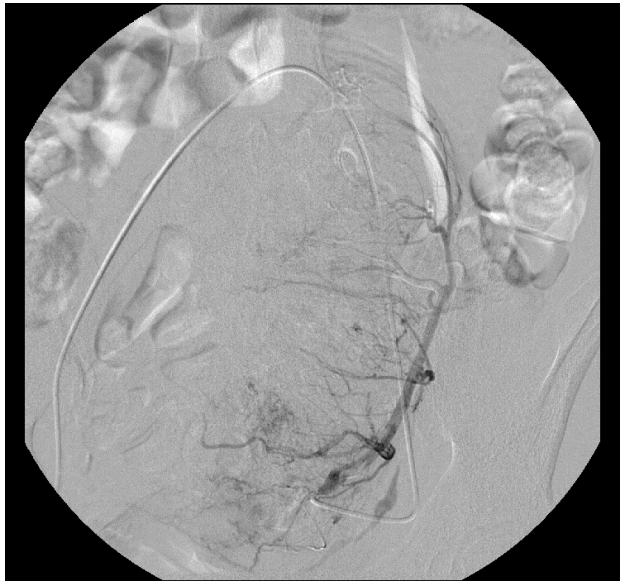
Uterine Artery Embolisation (UAE)

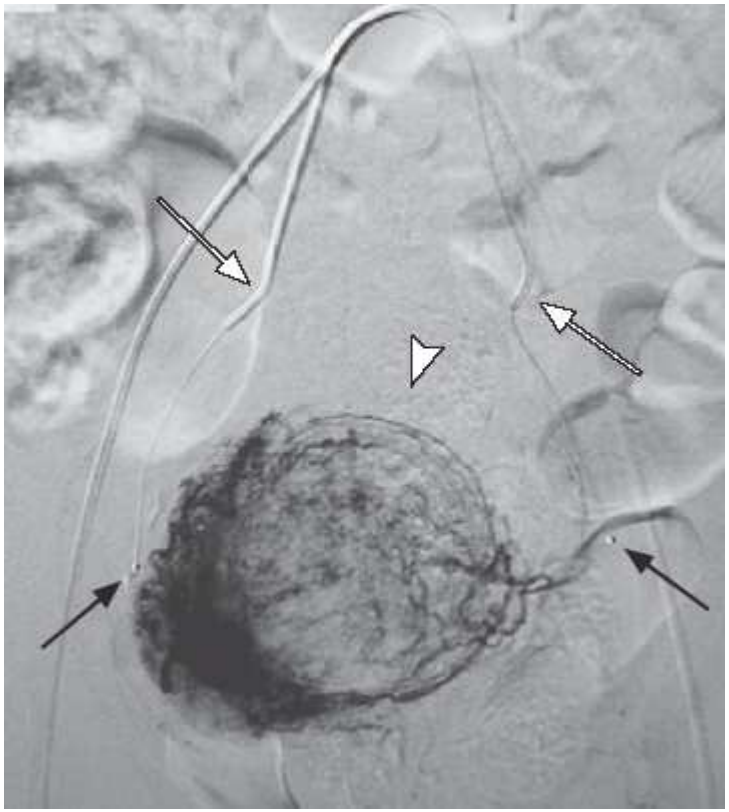


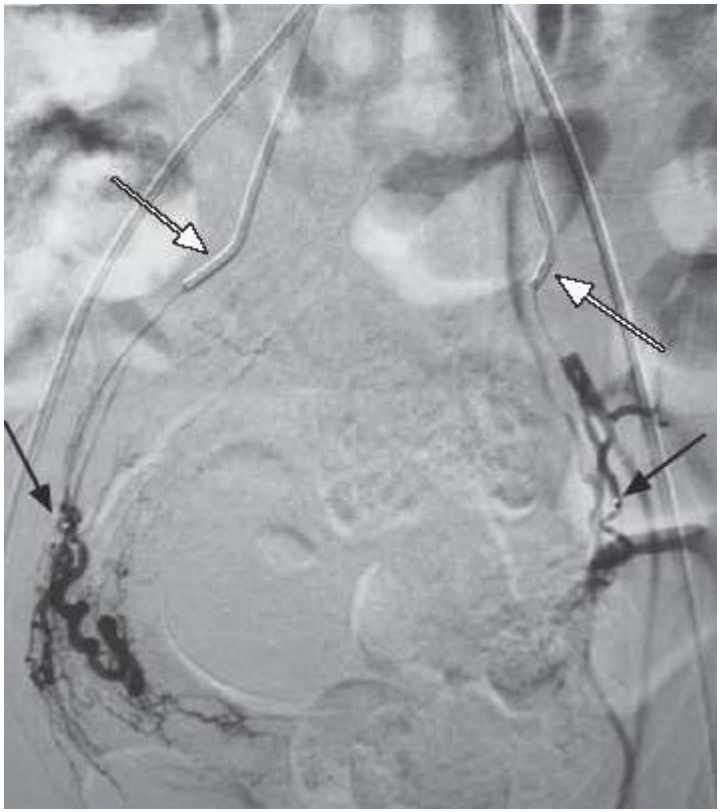


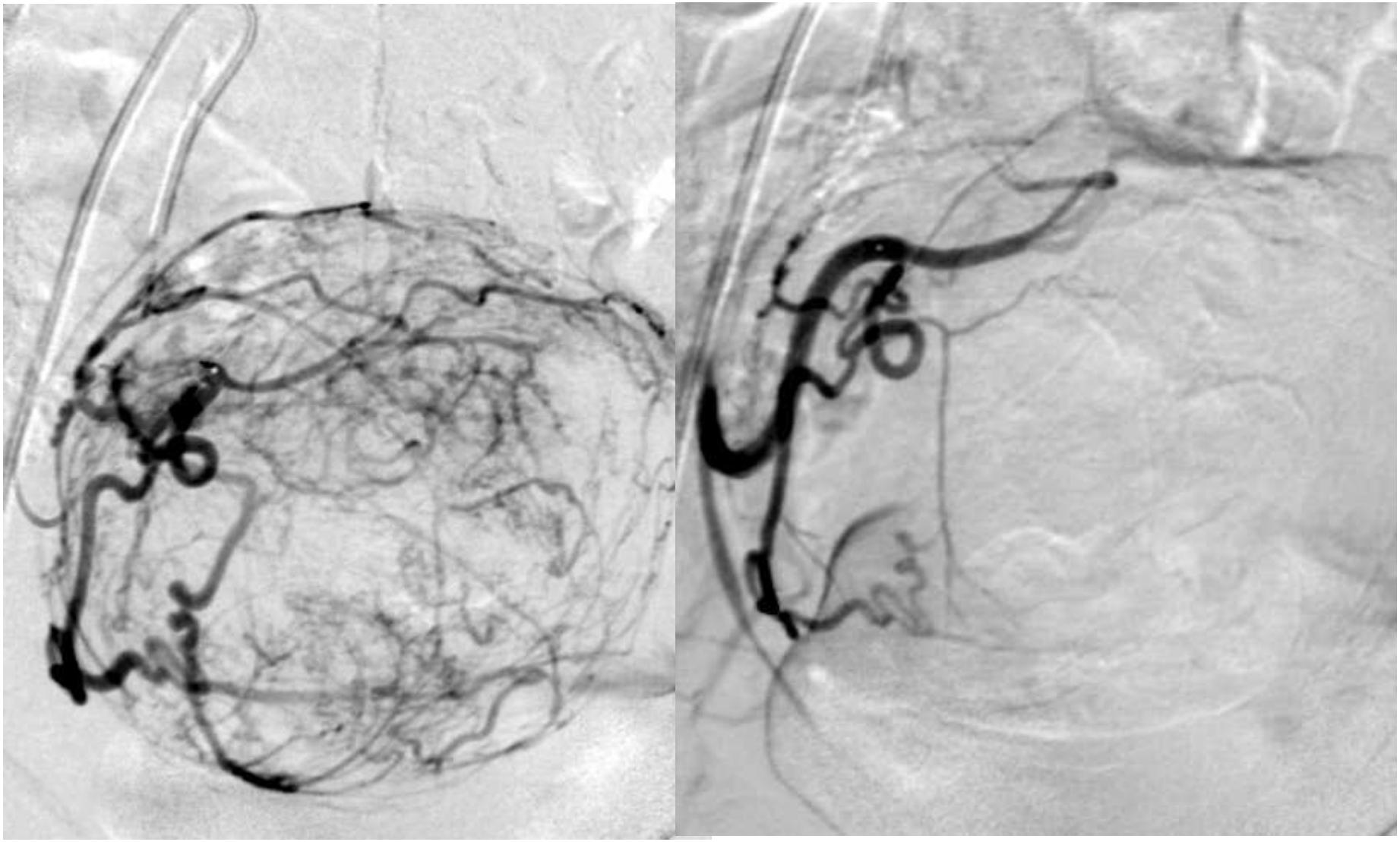
Polyvinylalkohol (PVA)

150-300 µm









selektiv A. uterina vor

post embo

Patientin kontrollierte Anästhsie

- Morphin - 2,5 mg Bolus i.v.
- Maximal 4 mal ein Bolus in einer Stunde
- Sperrintervall 5 – 10 minuten
- Antiemetikum

GUIDELINES

The American College of Obstetricians and Gynecologists (ACOG) concludes "based on good and consistent evidence (level A)" that "uterine artery embolization is a safe and effective option for appropriately selected women who wish to retain their uteri."[50] The ACOG also recommends caution when considering embolization in women who desire to retain their ability to conceive, because age-related amenorrhea can occur in a small minority of patients and because there is a possibility of abnormal placentation. The Society of Interventional Radiology and the Cardiovascular and Interventional Radiological Society of Europe state that uterine artery embolization "is indicated for the presence of uterine leiomyomata that are causing significant lifestyle-altering symptoms, specifically mass effect on the bladder or intestines, and/or dysfunctional uterine bleeding that is prolonged, associated with severe dysmenorrhea, or is causing severe anemia."[51]

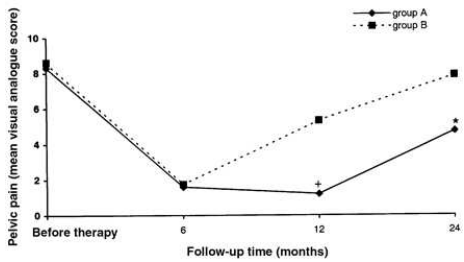
Since 1997, when uterine fibroid embolization was introduced into practice in the United States,[16] a number of large observational studies have been performed.[17-21] These studies have shown that menorrhagia is improved in 85 to 95% of patients, and similar rates of improvement have been noted with respect to pelvic pain, pressure, and urinary symptoms.

Goserelin

- **Br J Obstet Gynaecol 1999;106(7):672-7**
  - no therapy vs. goserelin (Zoladex®) s.c. q28x6
  - n=269; AFS II/IV; 24 mos
- **Ergebnis**
  - **weniger Rezidive n. 1a: 13% vs. 21%**
  - **weniger Rezidive n. 2a: 23% vs. 36%**
  - rezidivfreies Intervall sign. länger

Low-Dose Danazol

- **Hum Reprod 1999;14(9):2371-4**
- alle: surgery + GnRH-Analogon (triptorelin 3.75mg) q28x6
  - rand.: danazol 100mg/d f. 6 mos vs. no further therapy
  - n=28; AFS III/IV; 24 mos follow-up
- **Ergebnis**
  - **Schmerzscore besser p<0.01**
  - **Rezidive 44 vs. 67% p<0.05**
  - side effects gleich



GnRH + Anastrozol

- **Hum Reprod 2004;19(1):160-7**
  - OP + Goserelin 3.6mg q28x6 +/- Anastrozol 1mg/d 6 mos
  - n=97; severe endometriosis (rASRM score >40); 24 mos follow-up
- **Ergebnis**
  - länger rez.-frei 2.4 vs. 1.7 mos (p=0.009)
  - weniger Schmerzrezidive 35% vs. 8%
  - BMD-Verlust höher; QOL gleich

Ebert AD, Bartley J, David M.

Aromatase inhibitors and cyclooxygenase-2 (COX-2) inhibitors in endometriosis: new questions--old answers?

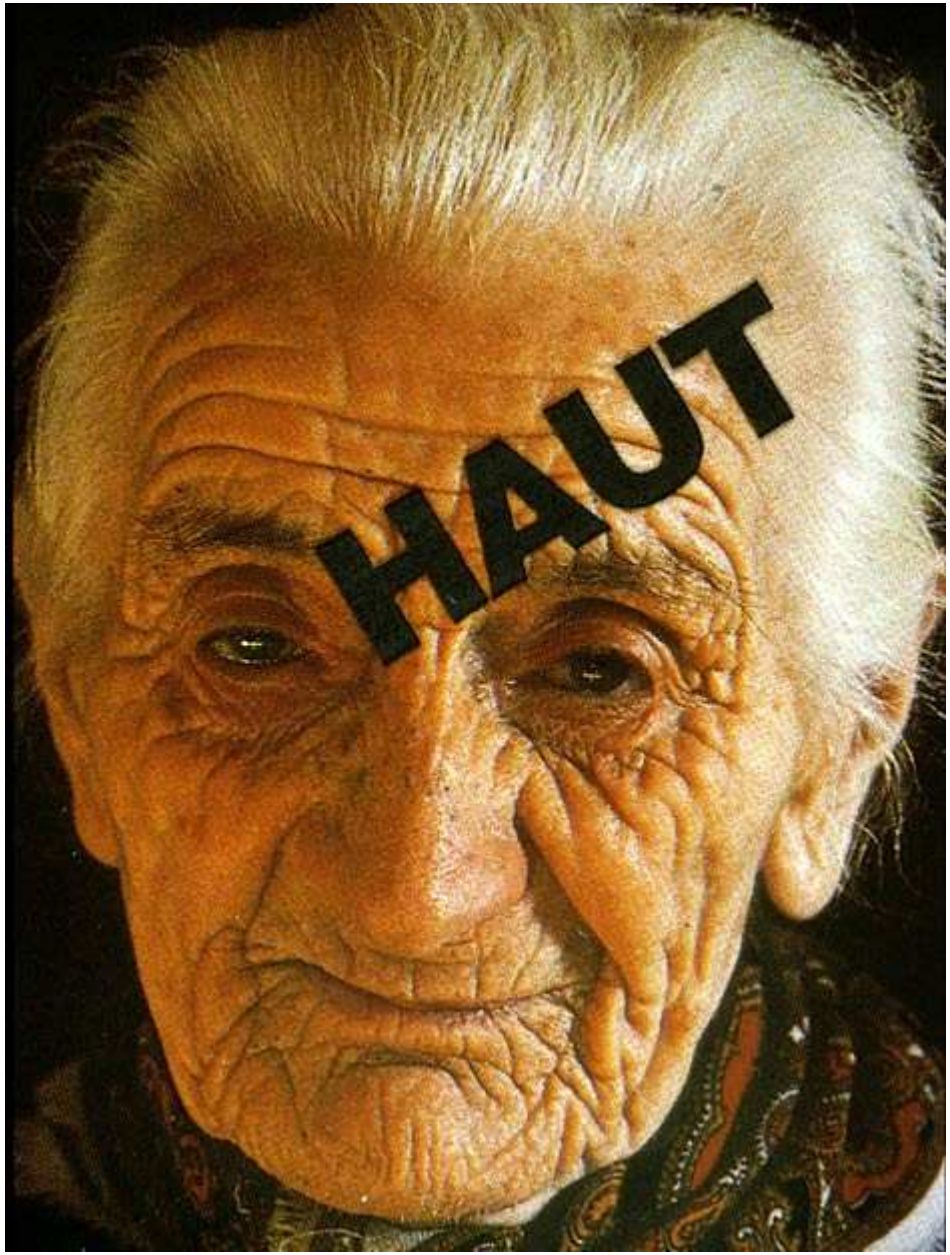
Eur J Obstet Gynecol Reprod Biol. 2005 Oct 1;122(2):144-50. Epub 2005 Sep 12.

Treatment:

Endpoints

Assessments

Hefler & Nagele


HAUT

The NEW ENGLAND JOURNAL of MEDICINE

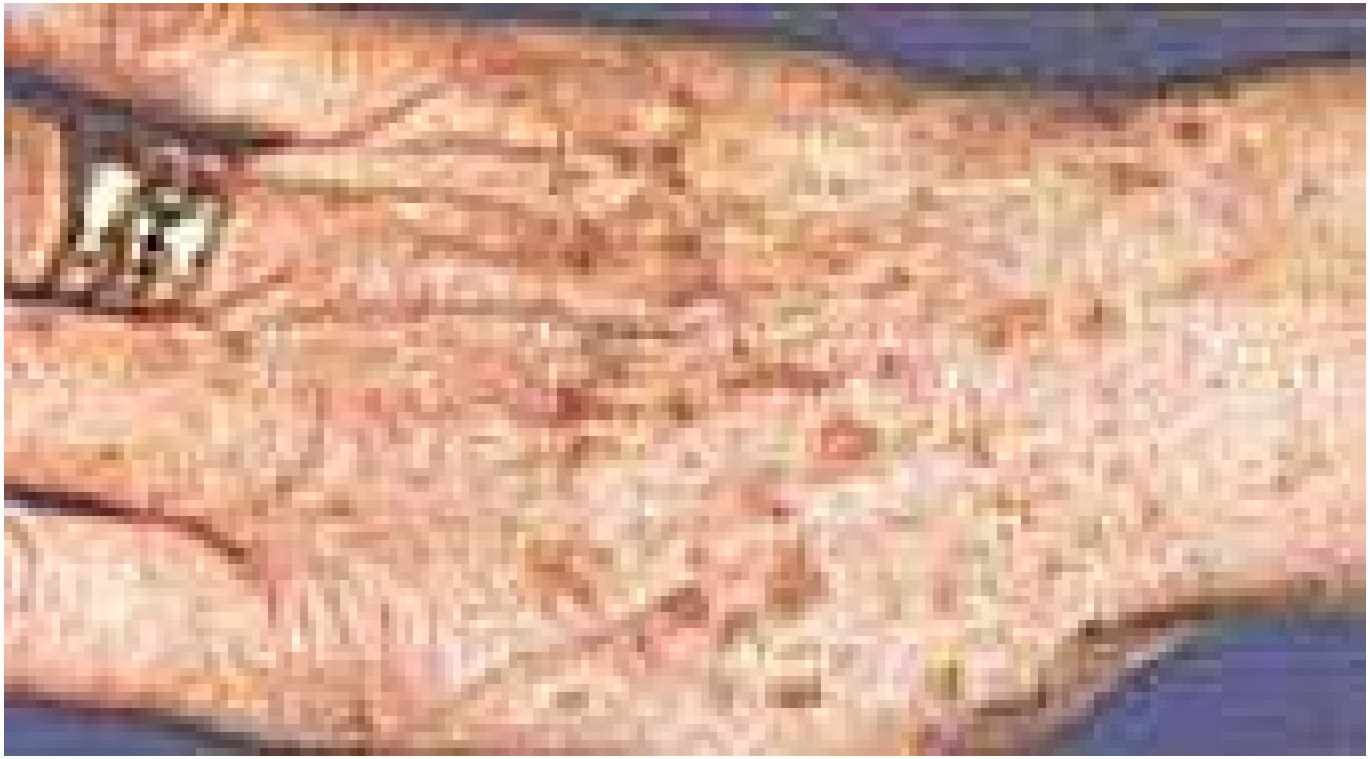
CLINICAL PRACTICE

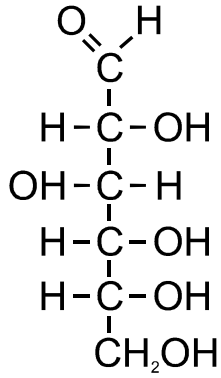
Treatment of Photoaging

Robert S. Stern, M.D.

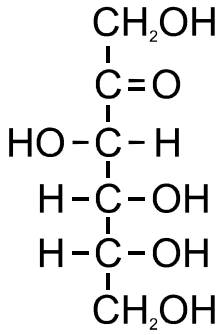
This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 45-year-old fair-skinned woman has noted increasing sallowness, roughness, fine wrinkles, and mottled hyperpigmentation on her face. She is bothered by these changes and is worried about the development of nonmelanoma skin cancer. What treatments may minimize skin aging and lower the risk of skin cancer?

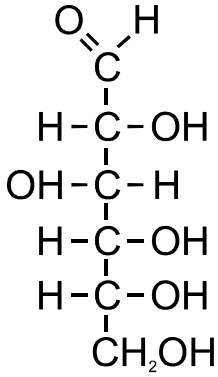




Glukose (Aldose)



Fruktose (Ketose)



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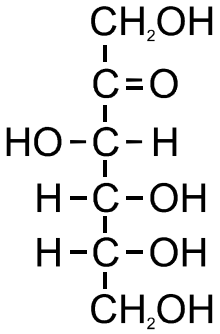
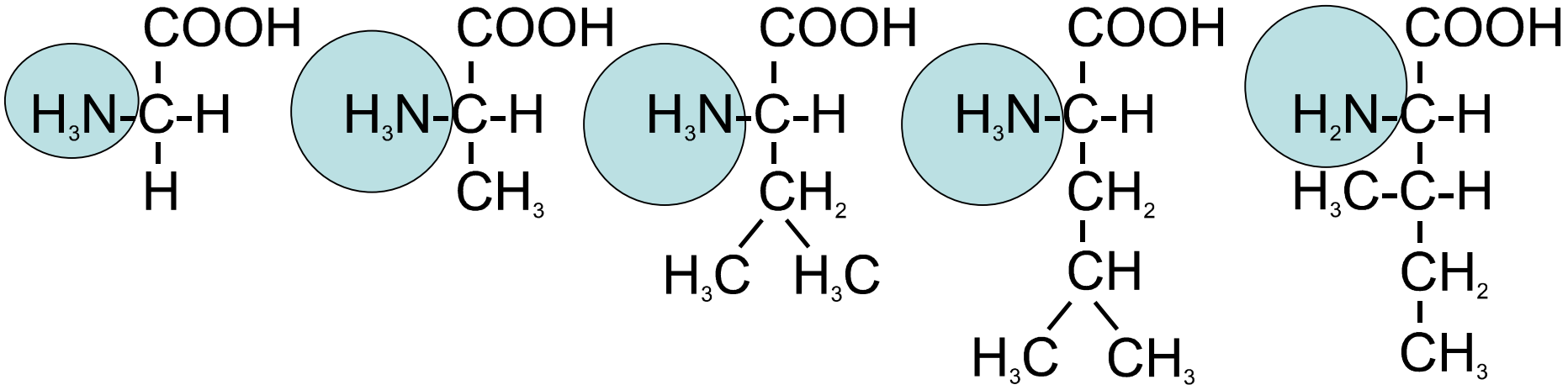
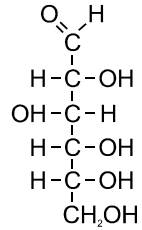


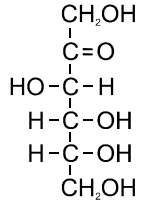
Fruktose (Ketose)



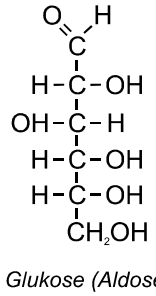
Glycin *Alanin* *Valin* *Leucin* *Isoleucin*



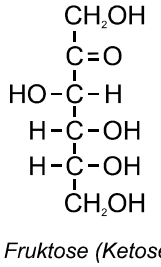
Glukose (Aldose)



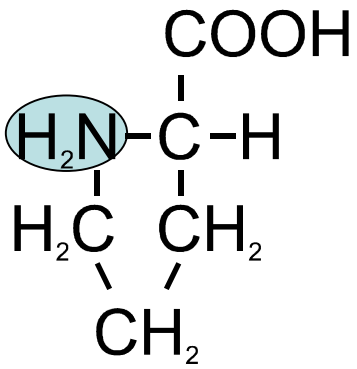
Fruktose (Ketose)



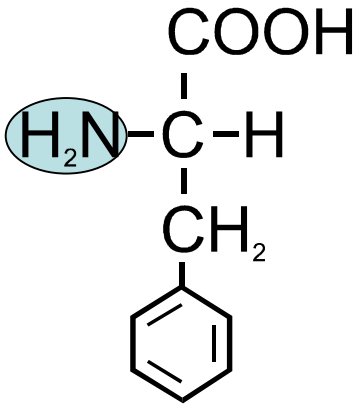
Glukose (Aldose)



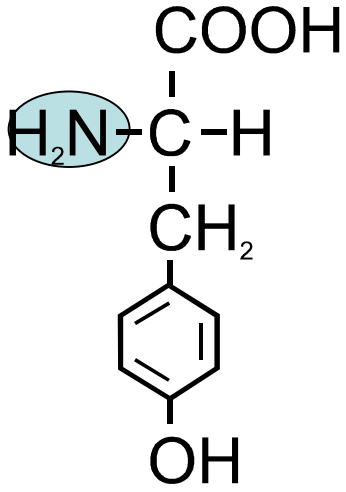
Fruktose (Ketose)



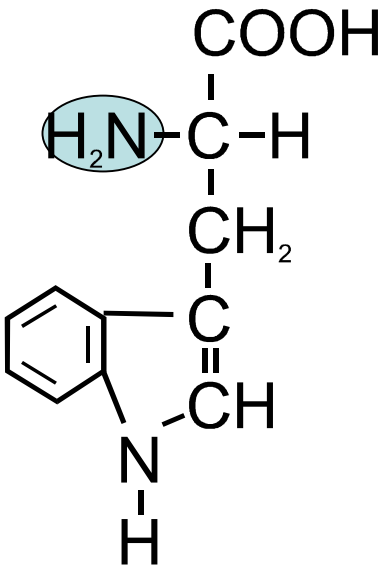
Prolin



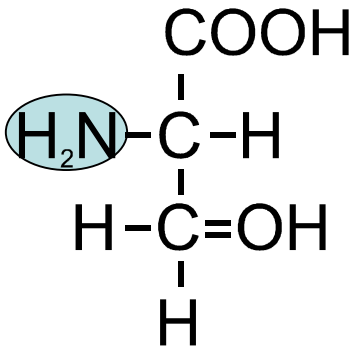
Phenylalanin



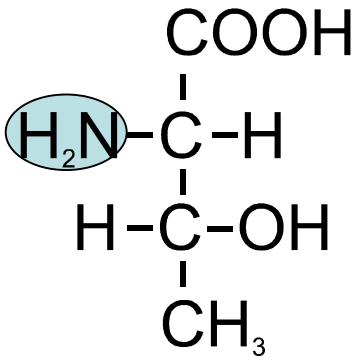
Tyrosin



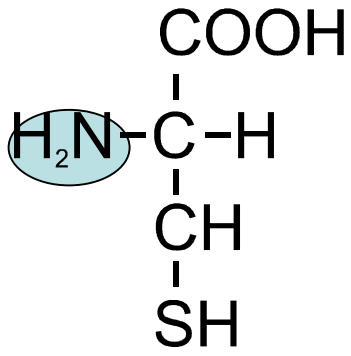
Tryptophan



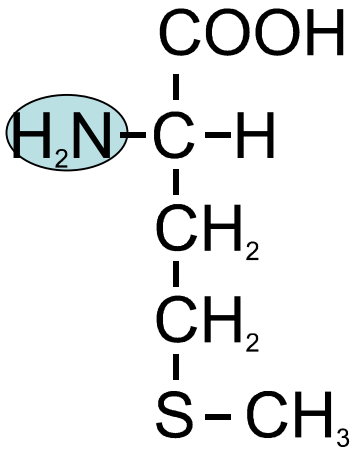
Serin



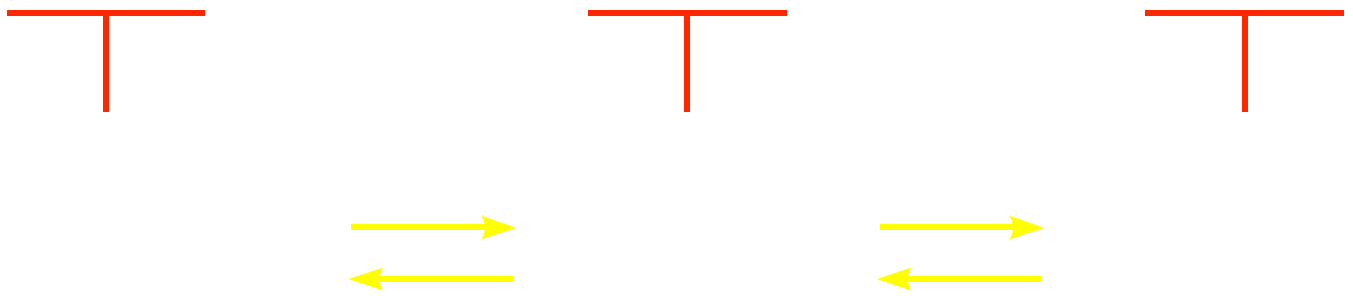
Threonin



Cystein



Methionin

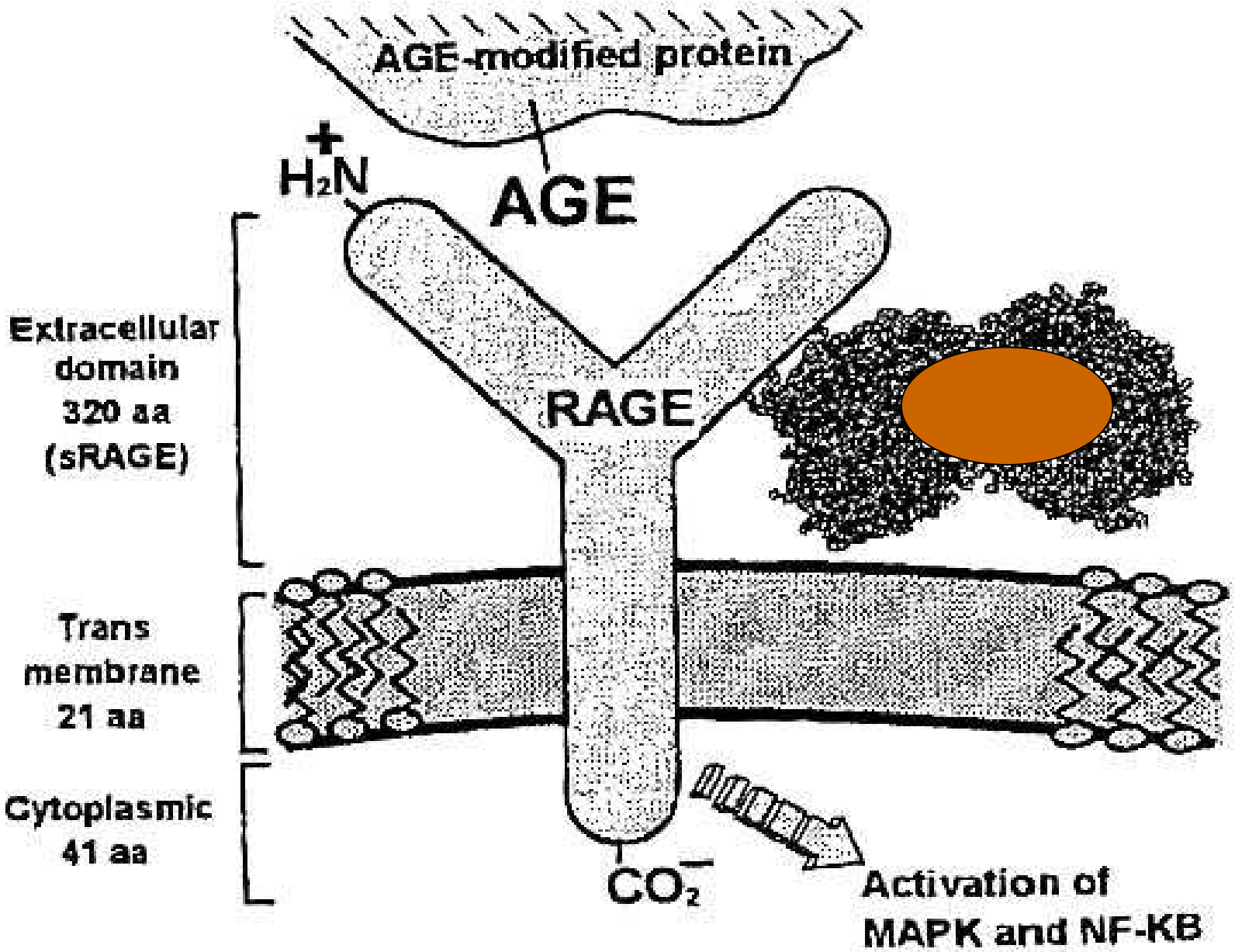

Schiffbase
Amadori

ALTERSBEDINGTE VERZUCKERUNG

MYELINSCHEIDEN

AUGENLINSE

HAUTKOLLAGEN


AGE-modified protein
AGE
H_2N
RAGE
Extracellular domain 320 aa (sRAGE)
Trans membrane 21 aa
Cytoplasmic 41 aa
CO_2^-
Activation of MAPK and NF-KB

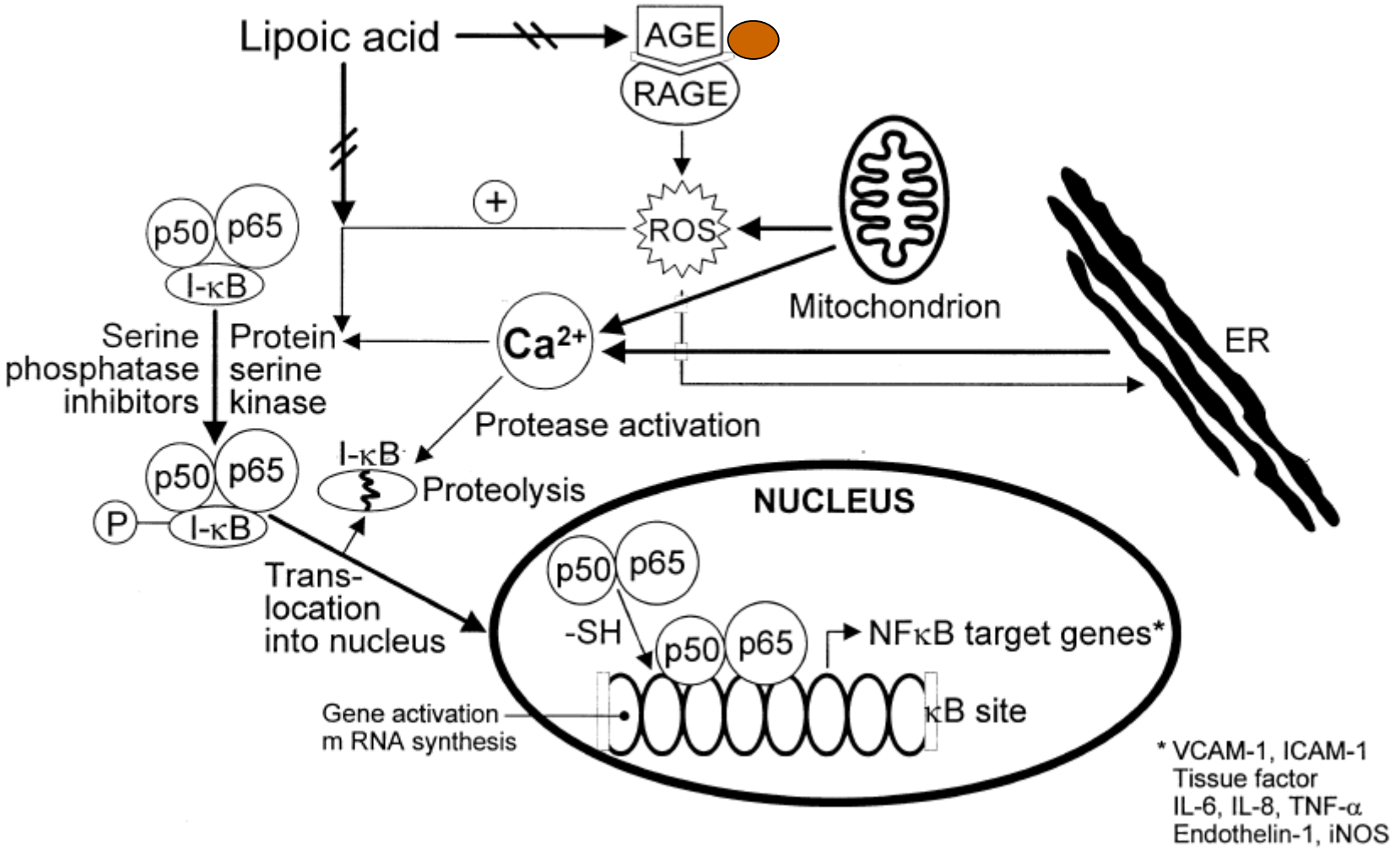
AGE

- INDUKTION PROINFLAMMATORISCHER PROTEINE

- VERLUST DER GEFÄSSELASTIZITÄT UND ANSPRECHBARKEIT AUF NO

- TISSUE FAKTOR UND NFKB ERHÖHT

Clin Geriatr Med. 2002 Aug;18(3):383-405. Review

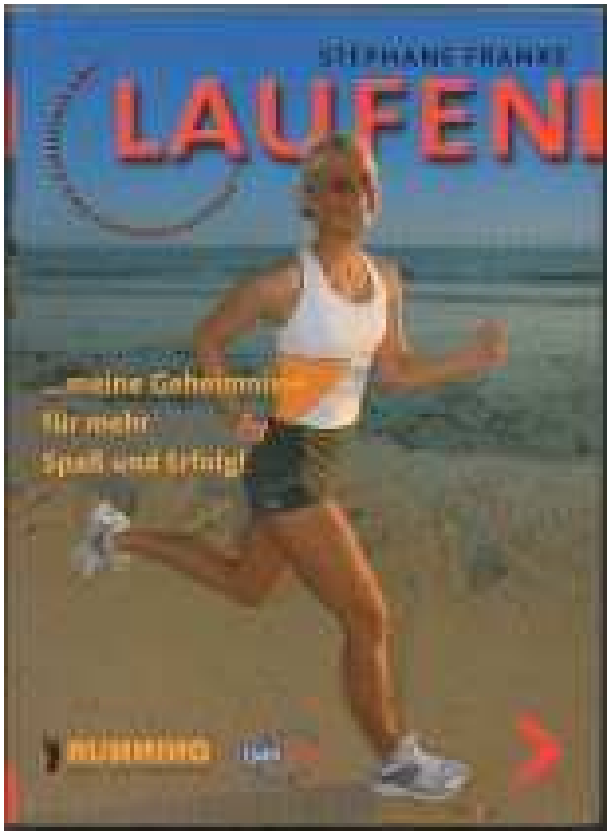

Lipoic acid
AGE
RAGE
ROS
+
p50
p65
I-κB
Mitochondrion
ER
Serine phosphatase inhibitors
Protein serine kinase
Ca2+
Protease activation
I-κB
Proteolysis
P
NUCLEUS
Trans-location into nucleus
-SH
NFκB target genes*
Gene activation
m RNA synthesis
κB site
* VCAM-1, ICAM-1
Tissue factor
IL-6, IL-8, TNF-α
Endothelin-1, iNOS

Vascular endothelial dysfunction in aging: loss of Akt-dependent endothelial nitric oxide synthase phosphorylation and partial restoration by (*R*)-α-lipoic acid

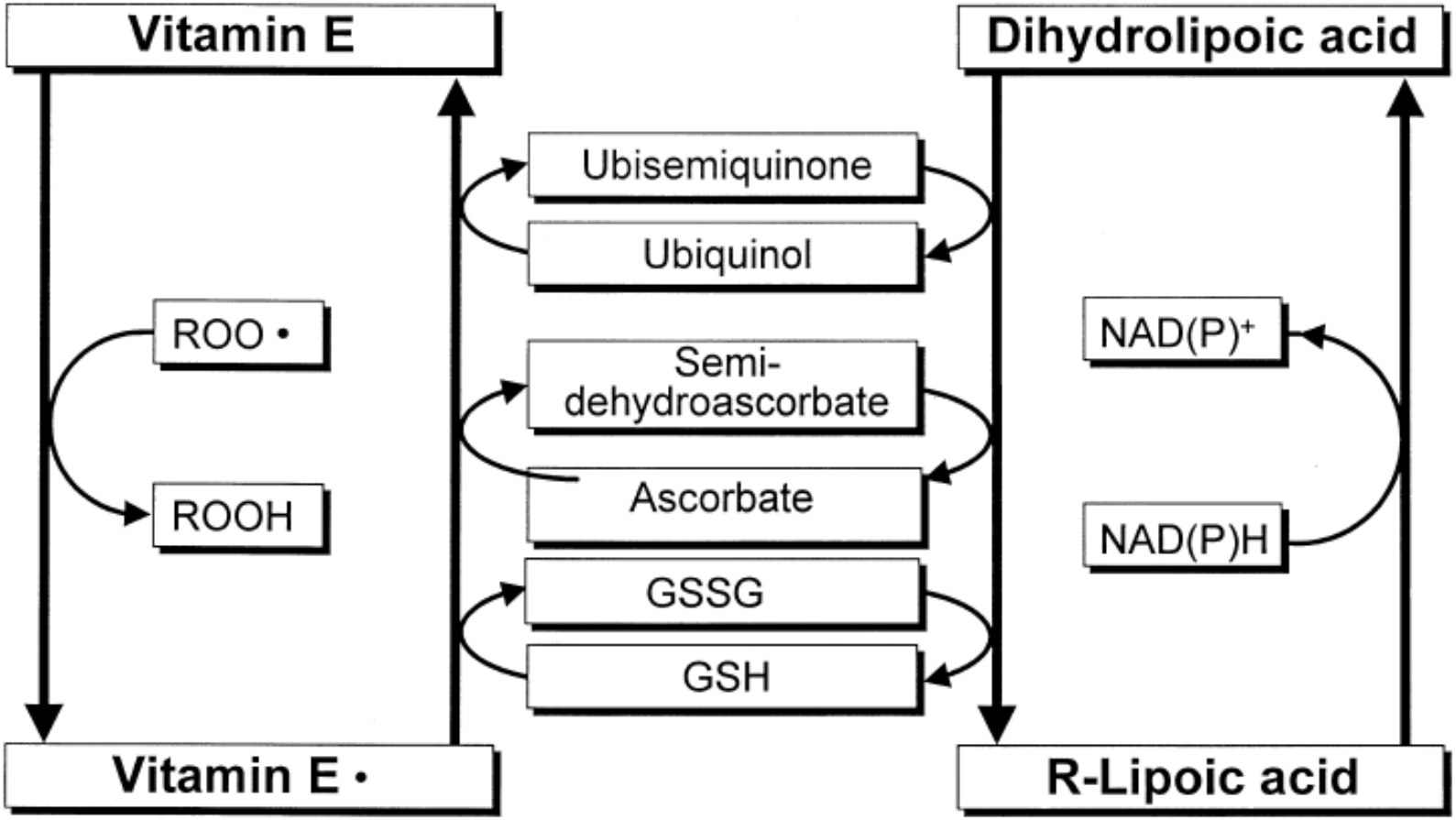
A.R. Smith and T.M. Hagen[1]

Department of Biochemistry and Biophysics and Linus Pauling Institute, 571 Weniger Hall, Oregon State University, Corvallis, OR 97331, U.S.A.

Molecular Mechanisms of Signalling



Radikalfänger
Glukosereduktion
Transkriptionsregulator


Vitamin E
Dihydrolipoic acid
Ubisemiquinone
Ubiquinol
ROO •
Semi-
dehydroascorbate
NAD(P)+
ROOH
Ascorbate
NAD(P)H
GSSG
GSH
Vitamin E •
R-Lipoic acid

British Journal of Dermatology 2003; **149:** 841–849.

Therapeutics

Randomized, placebo-controlled, double blind study on the clinical efficacy of a cream containing 5% α-lipoic acid related to photoageing of facial skin

H.BEITNER

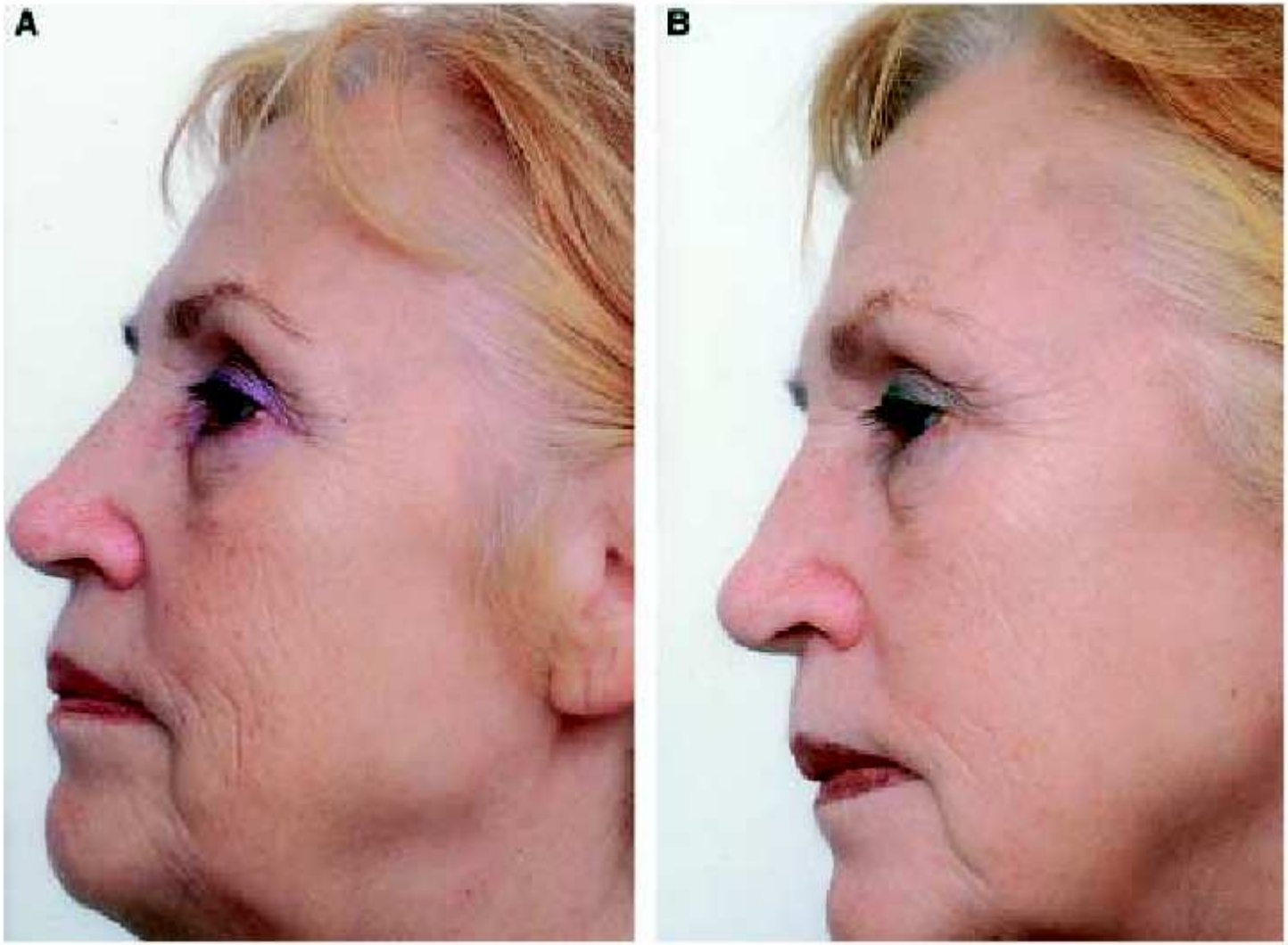
Department of Dermatology, Karolinska Hospital, 17176 Stockholm, Sweden

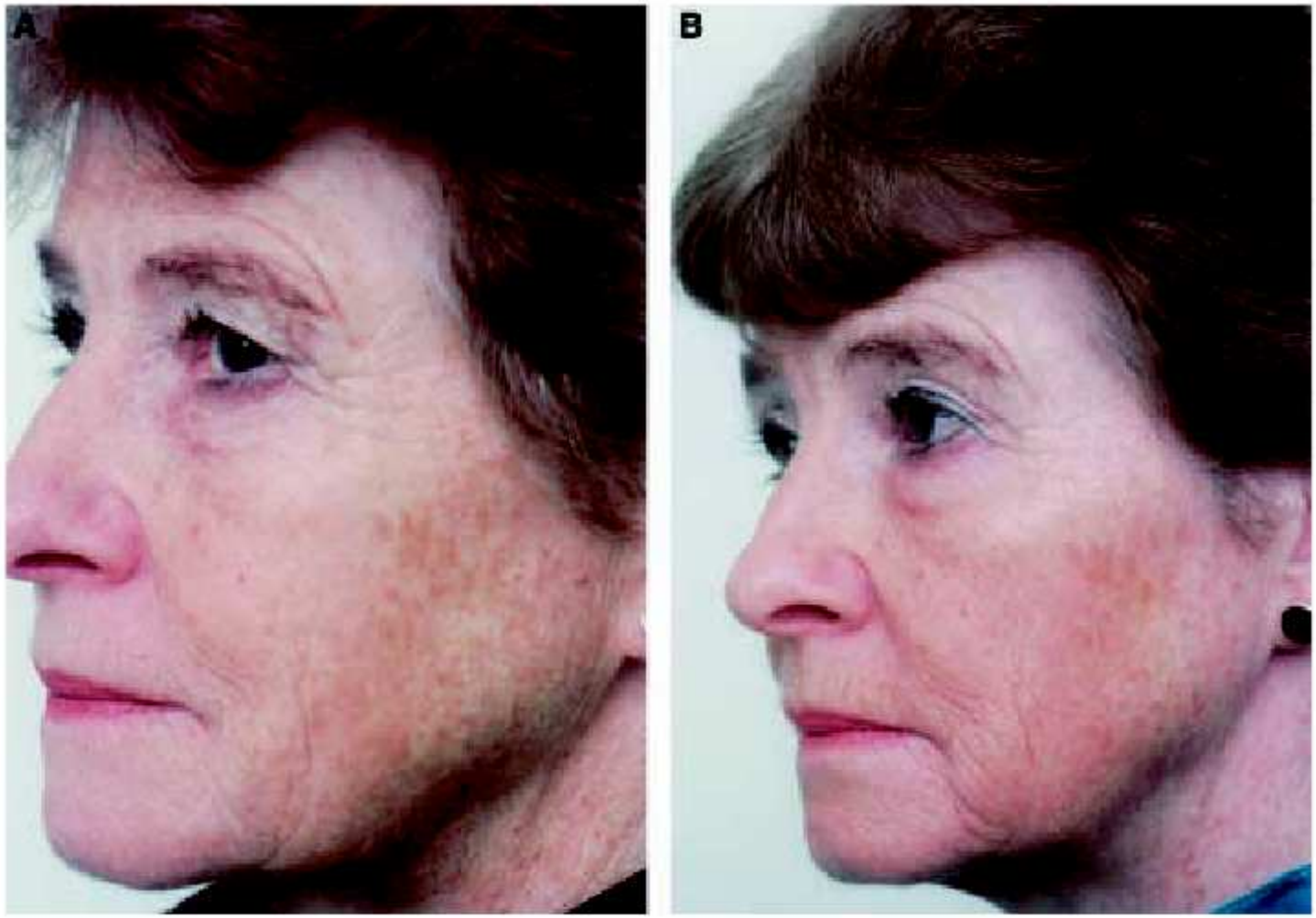
Br J Dermatol. 2003 Oct;149(4):841-9.

Randomized, placebo-controlled, double blind study on the clinical efficacy of a cream containing 5% alpha-lipoic acid related to photoageing of facial skin.

Beitner H.

CONCLUSIONS: It is indicated that 12 weeks of treatment with a cream


A
B


A
B

α LIPONSÄURE

AKNE-NARBEN

ROSAZEA

KOLLAGENVERLUST

TRÄNENSÄCKE


Skinrepair Maske
mit Alpha Liponsäure
für 10 Anwendungen 100ml
Ch.Nr.: 150311mk
zum alsbaldigen Gebrauch
Alte Leopoldsapotheke, Plankengasse 6, 1010 Wien


Hormonkosmetik
Prof.DDr.J.HUBER
Franz Eugen-Strasse 16


Hormonkosmetik
Prof.DDr.J.HUBER
Prinz-Eugen-Strasse 16
Skinrepair Maske
mit Alpha Liponsäure
für 10 Anwendungen 100ml

DOI 10.1111/j.1365-2133.2005.06685.x

Effects and side-effects of 2% progesterone cream on the skin of peri- and postmenopausal women: results from a double-blind, vehicle-controlled, randomized study

G. Holzer, E. Riegler, H. Hönigsmann, S. Farokhnia* and B. Schmidt

Division of Special and Environmental Dermatology, Medical University of Vienna, Währinger Gürtel 18–20, A-1090 Vienna, Austria
**Pharmacy Department, General Hospital of Vienna, Währinger Gürtel 18–20, A-1090 Vienna, Austria*

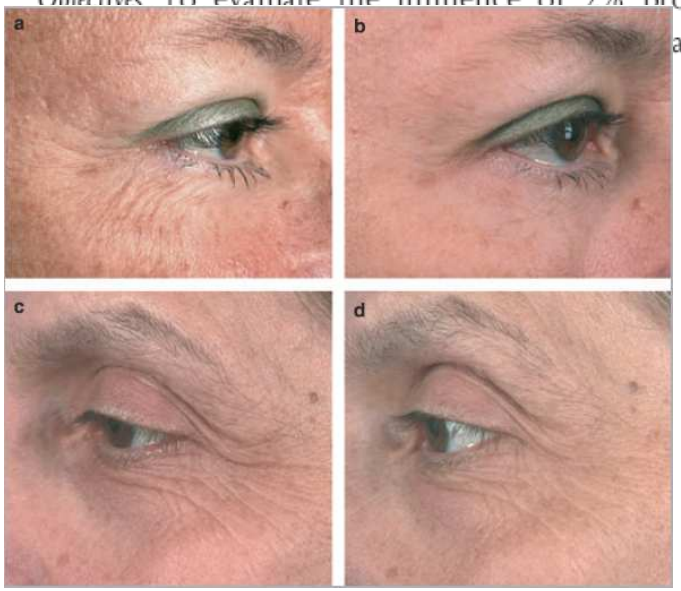
Summary

Correspondence
Dr Gregor Holzer.
E-mail: gregor.holzer@meduniwien.ac.at

Accepted for publication
12 January 2005

Background For many years topical progesterone has been prescribed by gynaecologists as an antiageing and skin-firming treatment, without any clinical scientific evidence of its effects, tolerability and safety when applied to skin.

Objectives To evaluate the influence of 2% progesterone cream on function and [illegible]al women.



PATHOPHYSIOLOGY OF PREMATURE SKIN AGING INDUCED BY ULTRAVIOLET LIGHT

GARY J. FISHER, PH.D., ZENGQUAN WANG, PH.D., SUBHASH C. DATTA, PH.D., JAMES VARANI, PH.D., SEWON KANG, M.D., AND JOHN J. VOORHEES, M.D.

ABSTRACT

Background Long-term exposure to ultraviolet irradiation from sunlight causes premature skin aging (photoaging), characterized in part by wrinkles, altered pigmentation, and loss of skin tone. Photoaged

ULTRAVIOLET irradiation from the sun has deleterious effects in human skin, including sunburn, immune suppression,[1] cancer, and premature aging (photoaging). Sunburn and immune suppression occur acute-

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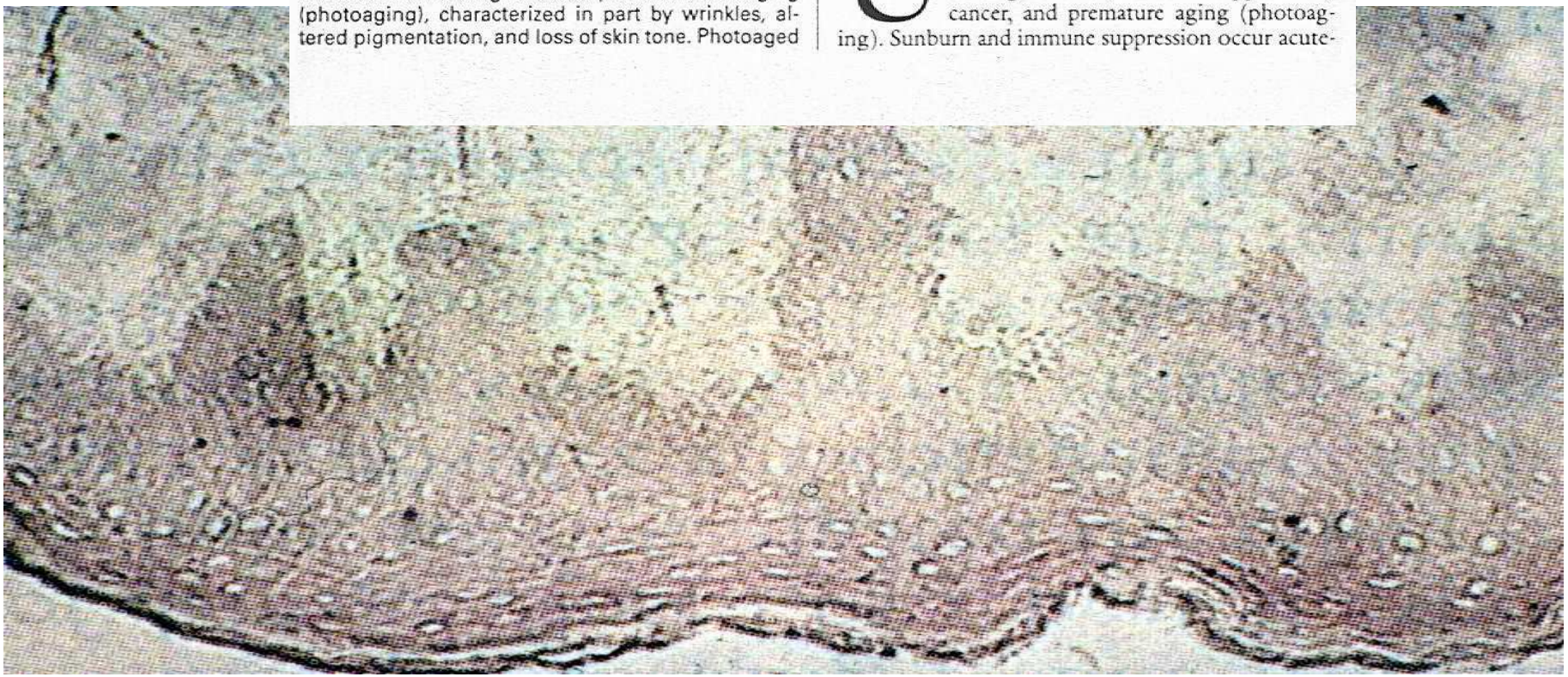

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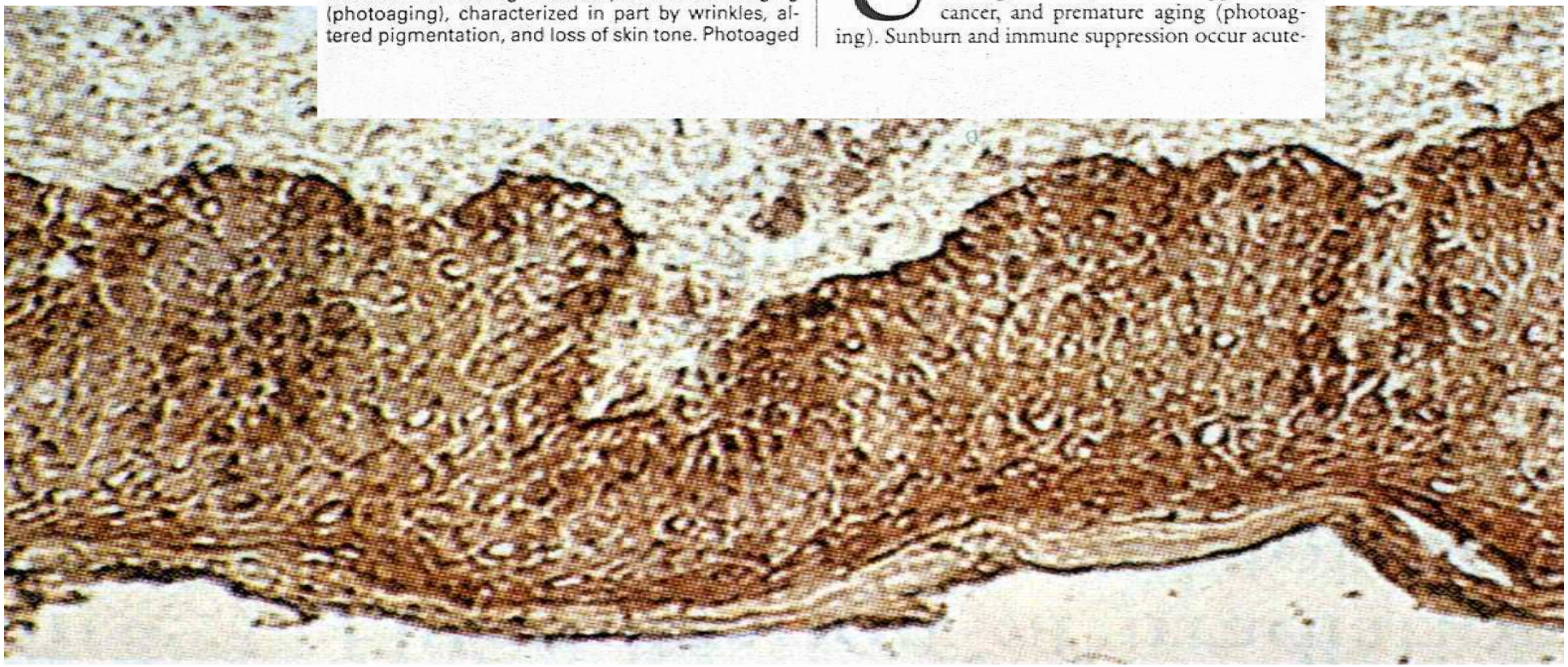
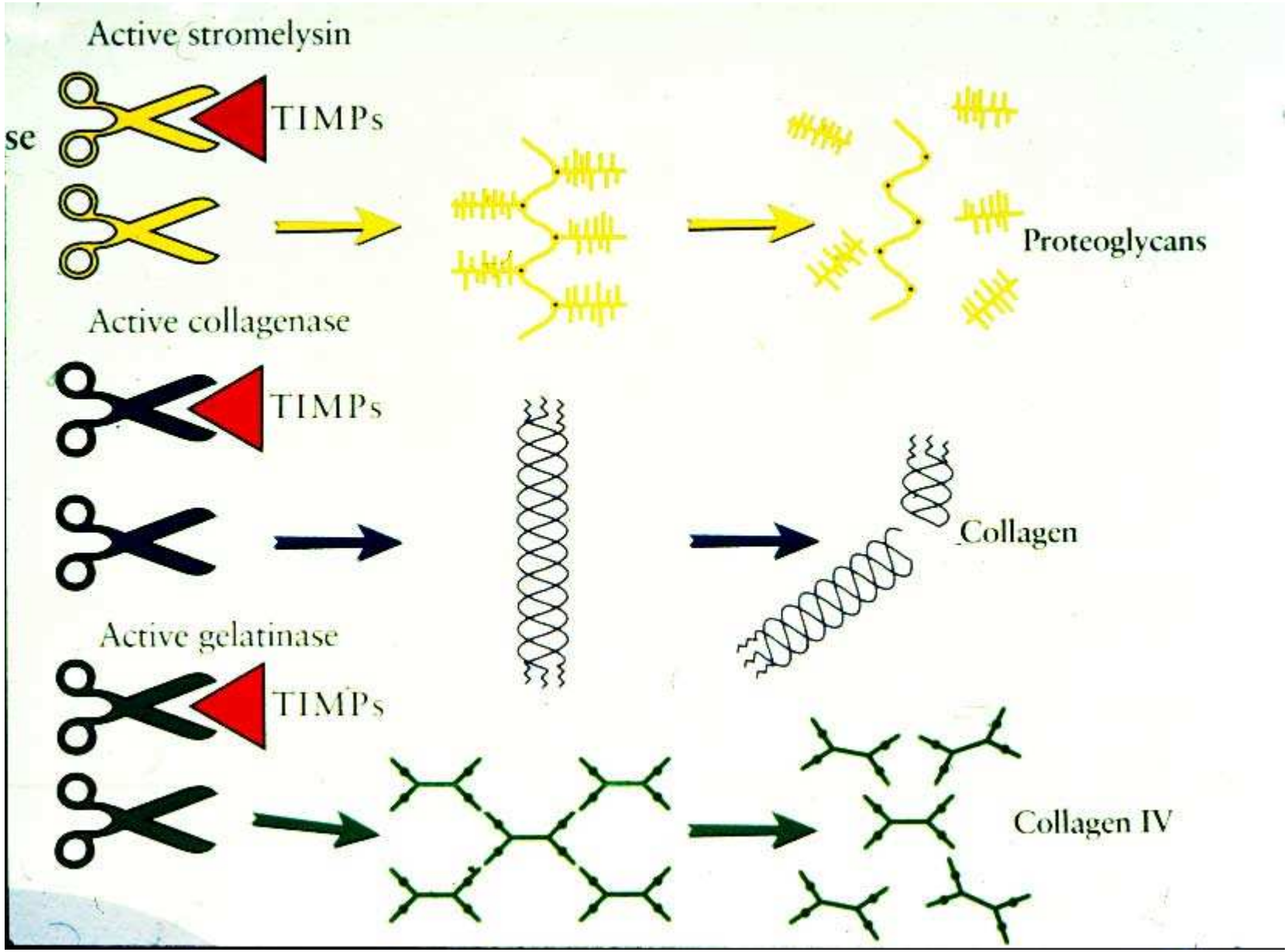


EVIDENCE THAT SMOKING CAUSES SKIN WRINKLING

We reviewed the English language literature published since 1960 and identified five studies that evaluated the association of cigarette smoking and skin wrinkling (table 1). Four of these five studies reported that white cigarette smokers were more wrinkled than nonsmokers (2–5). One study concluded


Active stromelysin
se
TIMPs
Proteoglycans
Active collagenase
TIMPs
Collagen
Active gelatinase
TIMPs
Collagen IV

British Journal of Obstetrics and Gynaecology
September 1997, Vol. 104, pp. 994–998

Analysis of collagen status in premenopausal nulliparous women with genuine stress incontinence

***Declan P. Keane** *Research Registrar*, †**Trevor J. Sims** *Chief Laboratory Technician*,
***Paul Abrams** *Consultant (Urology)*, †**Allen J. Bailey** *Professor*

**Bristol Urological Institute, Southmead Hospital, Bristol; †Muscle and Collagen Research Group, University of Bristol, Langford*

Objective To determine if differences exist in the collagen status of premenopausal nulliparous women with genuine stress incontinence compared with continent controls.

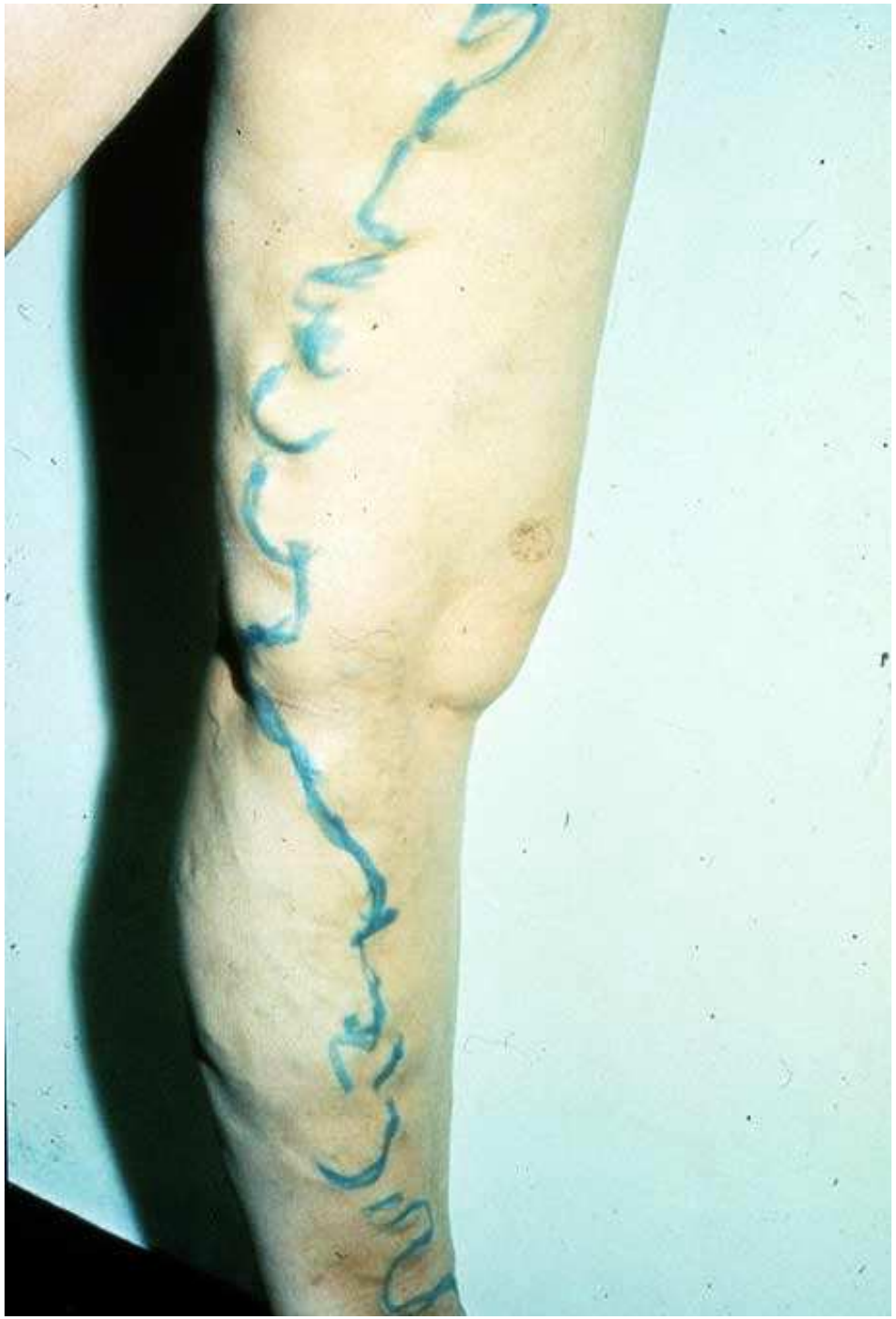
Design Thirty-six premenopausal nulliparous women with urodynamically-proven genuine stress incontinence were compared with 25 controls. All the women studied had a periurethral vaginal biopsy taken of approximately 30–50 mg in wet weight. This biopsy was then analysed to determine the collagen content, the type I:III collagen ratio and the collagen cross-link content.

Rp./

Progesteron	**1,00 g**
Propylenglykol	**5,00 g**
Jojobaöl	**5,00 g**
Cremegrundlage	**ad 50,00 g**

D.S. Progesteron Jojoba creame 2%

L´application topique de la progestérone pour le traitement de la peau



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DERMATOLOGIC THERAPY
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Esthetic and cosmetic dermatology

UWE WOLLINA*, ALBERTO GOLDMAN†, UWE BERGER‡ &
MOHAMMED BADAWY ABDEL-NASER§

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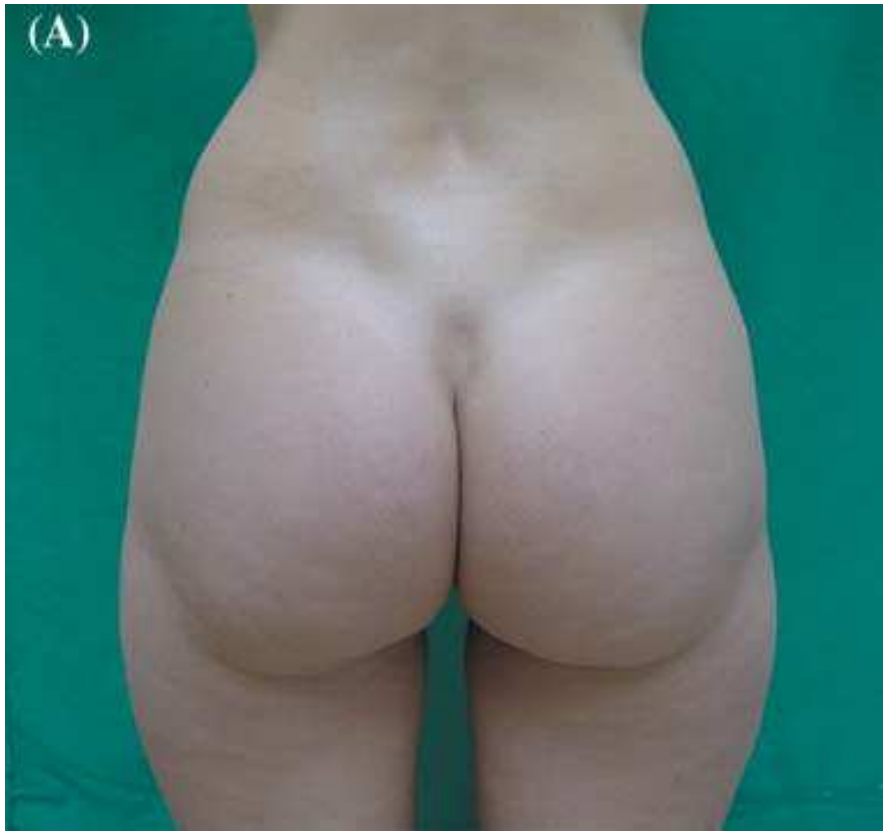

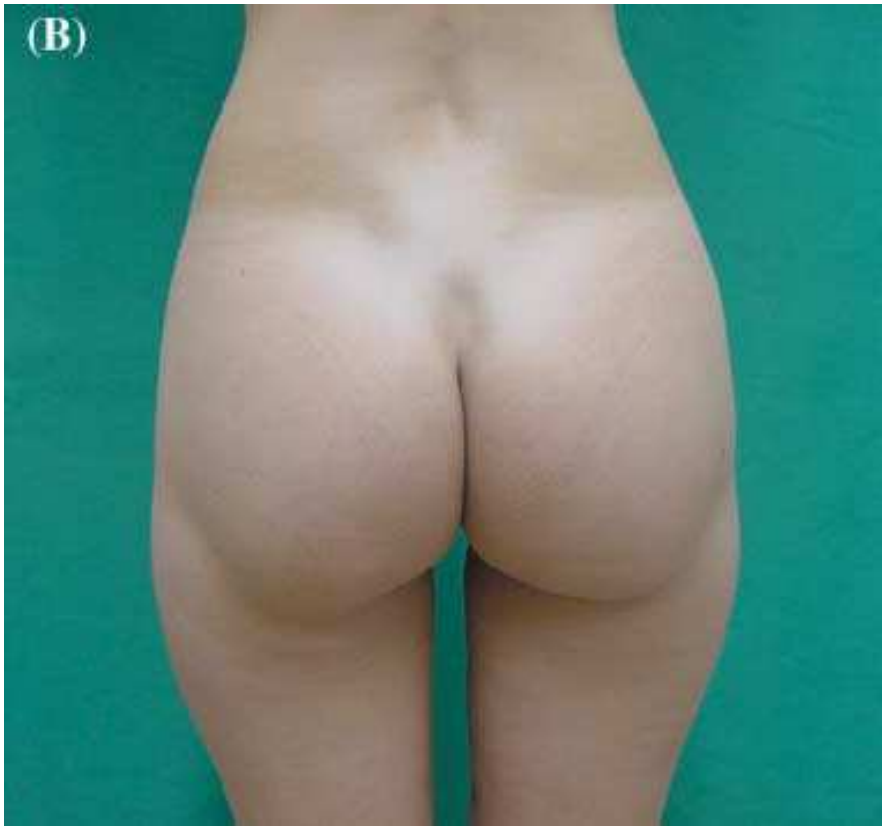

Modulation of Collagen Metabolism by the Topical Application of Dehydroepiandrosterone to Human Skin

Mi Hee Shin,[1] Gi-eun Rhie,[1] Chi-Hyun Park, Kyu Han Kim, Kwang Hyun Cho, Hee Chul Eun, and Jin Ho Chung

Department of Dermatology, Seoul National University College of Medicine and Laboratory of Cutaneous Aging Research, Clinical Research Institute, Seoul National University Hospital, Seoul, Korea

Dehydroepiandrosterone (DHEA) and its sulfate conjugate (DHEA-S) are the most abundantly produced human adrenal steroids to be reduced with age. DHEA may be related to the process of skin aging through the regulation and degradation of extracelluar matrix protein. In this study, we demonstrate that DHEA can increase procollagen synthesis and inhibit collagen degradation by decreasing matrix metalloproteinases (MMP)-1 synthesis and increasing tisuue inhibitor of matrix metalloprotease (TIMP-1) production in cultured dermal fibroblasts. DHEA was found to inhibit ultraviolet (UV)-induced MMP-1 production and the UV-induced decrease of procollagen synthesis, probably due to the inhibition of UV-induced AP-1 activity. DHEA (5%) in ethanol:olive oil (1:2) was topically applied to buttock skin of volunteers 12 times over 4 weeks, and was found to significantly increase the expression of procollagen α1(I) mRNA and protein in both aged and young skin. On the other hand, topical DHEA significantly decreased the basal expression of MMP-1 mRNA and protein, but increased the expression of TIMP-1 protein in aged skin. We also found that DHEA induced the expressions of transforming growth factor-β1 and connective tissue growth factor mRNA in cultured fibroblasts and aged skin, which may play a role in the DHEA-induced changes of procollagen and MMP-1 expression. Our results suggest the possibility of using DHEA as an anti-skin aging agent.

Key words: collagen/dermal fibroblast/DHEA/human skin/MMP-1/TIMP-1
J Invest Dermatol 124:315–323, 2005