

Lukić IK, Glunčić V, Ivkić G, Hubenstorf M, Marušić A.
Virtual dissection: a lesson from the 18th century. Lancet
2003;362:2110-13.

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The position and effect of anatomy have changed greatly over the centuries. Once a scientific empire and a foundation stone of medicine, it declined to a marginal and unattractive discipline. On the other hand, the ways to teach anatomy have become more sophisticated than ever. Over the centuries, classic dissection of a cadaver evolved to virtual dissection and computational anatomy. Despite these important changes, anatomy teaching retained the transmission of three-dimensional notions. In the past, such transmission was done with anatomical wax models, which were introduced as a didactic tool in the late 17th century and remained in use until the end of the 19th century. Although their historical and artistic value was subject to much research, they were not assessed for their anatomical value, as a reflection of the anatomical knowledge and ideas of their time. Here, we present our analysis of 867 models on display in one of most famous anatomical wax model collections—the Josephinum Wax Models Museum, Vienna, Austria. The Florentine masters and their wax models teach us that we have to appreciate the knowledge of anatomy even more than they did—sound knowledge of anatomy is the best defence against incorporating morphological misunderstandings and biases into clinical practice.

**Đurić K, Škrablin S, Lesin J, Kalafatić D, Kuvačić I,
 Suchanek E. Second trimester total human chorionic
 gonadotropin, alpha-fetoprotein and unconjugated estriol in
 predicting pregnancy complications other than fetal
 aneuploidy. Eur J Obstet Gynecol Reprod Biol**
2003;110:12-5.

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The aim of this study was to assess the value of alpha-fetoprotein (AFP), total human chorionic gonadotropin (ThCG) and unconjugated estriol in predicting certain complications of pregnancy other than fetal aneuploidy. Among 2384 women that underwent biochemical screening between 15 and 22 weeks of gestation, pregnancy outcome was evaluated in 677 women under 35 years of age according to serum marker levels by using cut-off points discriminative for Down syndrome or neural tube defect (NTD). High AFP levels (MoM 2.0) were found to be significantly more frequent ($p < 0.05$) in cases of fetal growth restriction (odds ratio=2.7), miscarriage (odds ratio=4.4) and intrauterine fetal death (odds ratio=5.8). High ThCG levels (MoM 2.02) were associated with intrauterine growth restriction (odds ratio=2.1; $p < 0.05$), miscarriage (odds ratio=4; $p < 0.01$), preterm birth (odds ratio=2.5; $p < 0.05$), and intrauterine fetal death (odds ratio=4.2; $p < 0.01$). Among pregnancies with intrauterine growth restriction and threatening preterm delivery, low unconjugated estriol levels (MoM 0.74) were significantly more frequent (odds ratio=2.2; $p < 0.05$ and odds ratio=2.6; $p < 0.01$, respectively). In conclusion, all three markers predictive for fetal trisomy 21 shown

to be associated with various pregnancy complications in euploid pregnancies.

***Gagro A, Toellner KM, Grafton G, Servis D, Branica S,
 Radojčić V, Kosor E, et al. Naive and memory B cells
 respond differentially to T-dependent signaling but display
 an equal potential for differentiation toward the
 centroblast-restricted CD77/globotriaosylceramide
 phenotype. Eur J Immunol 2003;33:1889-98.**

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Resting (CD38low) tonsillar B cells differentiate to express the centroblast-restricted CD77/globotriaosylceramide antigen on high-level engagement of CD154. As the CD38low population comprises both naive and memory subsets, the authors wished to compare the propensity of each to develop this germinal centre phenotype; particularly as the capacity of memory B cells to re-enter a follicular reaction remains unclear. Resting B lymphocytes were therefore separated into CD27-IgA-IgG- and IgD- fractions to generate subsets enriched for naive and memory cells, respectively. Following stimulation via BCR and/or CD40 - surrogate signals for B cells engaged in T-dependent signalling - differences between the two subsets were seen in the kinetics and/or magnitude of responses such as entry into DNA synthesis, induction of the co-stimulatory molecules CD80 and CD86; up-regulation of CD23, and changes in BCL-6 mRNA expression. Nevertheless, naive and memory cells revealed a high identical capacity for acquiring CD77: both appeared equally sensitive in this regard, with high-level CD40 engagement via cell-bound CD154 being required for both subsets to achieve the hallmark centroblast phenotype. These findings suggest that, provided with the opportunity to encounter cell membrane CD154 in abundance, both naive and memory B cells display the potential to be diverted towards a germinal centre pathway of differentiation.

***Jonjić N, Zamolo G, Štifter S, Fućkar D, Gruber F, Sasso F,
 et al. Cytomorphological variations, proliferation and
 angiogenesis in the prognosis of cutaneous melanoma. Clin
 Exp Dermatol 2003;28(3):310-4.**

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 Medicine and Hospital Center, Rijeka, Croatia*

The aim of this study was to analyse proliferation by mitotic activity index (MAI) and immunostaining of proliferating cell nuclear antigen (PCNA), and the intensity of neovascularization (microvessel density; MVD) in cutaneous melanoma (CM) clinical stage I in relation to epithelioid, spindle and nevoid cell type, histological type (superficial spreading melanoma and nodular melanoma), Clark's level and Breslow thickness. Finally, the role of all parameters in the prognosis of CM was evaluated. Statistical analysis demonstrated that cytological characteristics of CM correlate only with Clark's level, while histological types correlate with MAI, PCNA and MVD. MAI and PCNA also showed correlation between groups according to Clark's level and Breslow thickness. Finally, tumour cell PCNA was found to correlate with MVD. Survival of patients with CM correlated significantly with MAI. These results suggest that cytological variation, histological type, PCNA and MVD

alone are not independent prognostic parameters, whereas MAI is a potentially important prognostic marker in CM.

***Krušlin B, Tomas D, Rogatsch H, Novosel I, Čupić H, Belicza M, et al. Periacinar retraction clefting in the prostatic needle core biopsies: an important diagnostic criterion or a simple artifact? *Virchows Arch* 2003;443:524-7.**

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The diagnosis of prostatic adenocarcinoma in needle core biopsy is based on major and supportive criteria. One of the supportive criteria is the presence of retraction clefting around neoplastic glands. The authors analyzed a series of 137 prostatic cancer cases diagnosed by needle core biopsy to determine the frequency, extent and criteria for periacinar retraction clefting. Clefting was analyzed on ten neoplastic and ten normal glands in three different high power fields. One-third or more glands with clefts affecting more than 50% of circumference were significantly more common in tumors (51.8%) than in benign glands (8%) ($p < 0.0001$). A stricter criterion that designated as positive the cases with at least 50% of neoplastic glands (15 of 30) with clefts that affected more than 50% of circumference revealed clefts in only 15.3% of the malignant cases but none in benign cases (0%) ($p < 0.0001$). Regardless of their extension, 15 or more glands with clefts were also more prominent in malignant cases (86.9%) than in benign cases (20.4%) ($p < 0.0001$). The authors conclude that periacinar retraction clefting represents a reliable criterion for diagnosis of the prostatic adenocarcinoma, especially in cases with clefts affecting more than 50% of circumference in at least 50% of suspicious glands.

Čulić V, Mirić D, Jukić I. Acute myocardial infarction: differing preinfarction and clinical features according to infarct site and gender. *Int J Cardiol* 2003;90:189-96.

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Electrocardiographically determined infarct site, demographic and clinical variables were prospectively recorded for 1623 consecutive patients admitted to Clinical Hospital Split between 1990 and 1994 due to a first Q-wave acute myocardial infarction. Anterior infarctions were correlated with a higher prevalence of diabetes ($p = 4 \times 10^{-6}$) or pulmonary venous congestion ($p = 2 \times 10^{-12}$); inferior infarctions were correlated with a lower prevalence of hypertension ($p = 0.001$), hypercholesterolemia ($p = 0.02$) or diabetes ($p = 10^{-5}$), and a higher prevalence of smoking ($p = 0.001$); lateral infarctions were characterised by a smaller infarction size and lower prevalence of pulmonary congestion ($p = 0.002$). Among men under the age of 50 with inferior infarction there were 90% smokers, which was significantly more than among their gender ($p = 0.005$) or infarct site ($p = 2 \times 10^{-5}$) counterparts. After adjustment for age and other confounding factors, the prevalence of inferior infarction was higher in men ($p = 0.002$). Increased age ($p = 0.002$), female gender ($p = 0.0006$), anterior site ($p = 10^{-5}$), diabetes ($p = 0.0003$), greater creatine kinase-MB fraction level ($p = 0.001$) and pulmonary congestion ($p = 9 \times 10^{-6}$) were independent predictors of an adverse hospital outcome. Each site of acute myocardial infarction has relatively specific preinfarction and clinical features. These results suggest a greater importance of vasoconstriction in the pathophysiology of inferior infarction, especially in young male smokers, and greater importance of advanced atherosclerotic process in occurrence of anterior infarction.

Ferle-Vidović A, Jukić I, Škare D, Šuman L, Vuković L. Radioprotective and antitumor activity evaluation of newly synthesized adamantyl tenocyclidines. *Cancer Biother Radiopharm* 2003;18:781-90.

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Several adamantyl derivatives of thienyl phencyclidine (tenocyclidine; TCP) were newly synthesized and characterized:

adamantyl derivatives containing piperidine (TAPIP), pyrrolidine (TAPYR), and morpholine (TAMORPH) groups. Their biological activity was evaluated by in vitro testing of their effect on the proliferative and reproductive ability (cytotoxicity) of a human tumor cell strain and nonmalignant mouse fibroblasts in culture. The compounds were also tested for their radioprotective effect after ionizing irradiation, and as anticancer agents on the same human tumor cell strain. Compared with TCP, adamantyl derivatives are less toxic and have outstanding radioprotective properties. These derivatives (especially TAMORPH) increase apoptotic death of human malignant cells. The radiation-modifying effect studied on C3Hf mice in vivo showed that the adamantyl derivatives of TCP have a more enhanced radioprotective effect and that they are less toxic than TCP itself.

Đapić T, Kušec V, Jelić M, Vukičević S, Pečina M. Compressed homologous cancellous bone and bone morphogenetic protein (BMP)-7 or bone marrow accelerate healing of long-bone critical defects. *Int Orthop* 2003;27:326-30.

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The authors studied 18 adult male New Zealand rabbits with a critical right-sided ulnar defect of 15 mm. In six animals the defect was grafted with homologous compressed cancellous bone, in six animals with homologous compressed cancellous bone including 300 μ g bone morphogenetic protein (BMP)-7 and in six animals with homologous compressed cancellous bone including 0.5 ml autologous bone marrow. The defect was studied using radiographs every second week for 10 weeks. At the conclusion of the experiment the animals were killed and the defect studied by histology and histomorphometry. In all animals treated with the addition of autologous bone marrow and in five of six animals treated with the addition of BMP-7, the defect healed. There was no union in animals treated with homologous compressed cancellous bone without additive. The histological picture of the regenerated area was similar in the two experimental groups. Woven bone contained small marrow spaces with fibrous tissue and capillaries. The osteoid seams were on average greater in animals that received autologous bone marrow as compared to animals that received BMP-7.

Krmpotić-Nemanić J, Vinter I. Missing and incorrect terms in *Terminologia Anatomica* (1998). *Ann Anat* 2003;185:387-8.

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The authors suggest that the term articulation femoropatellaris should be introduced in the new anatomic terminology, because of the importance of this entity in the function and pathology of the knee joint. In order to indicate that the condylar surfaces, having a different function are separated from the patellar surface of the femur, the term "linea condylopatellaris medialis and linea condylopatellaris lateralis" should be introduced in the anatomical terminology. The term "nodus lymphoideus" should be changed to nodus lymphaticus because the adjective lymphaticus means belonging to the node in question while the adjective lymphoideus means "similar", which is not correct.

***Katavić V, Grčević D, Lee SK, Kalinowski J, Jastrzebski S, Dougall W, et al. The surface antigen CD45R identifies a population of estrogen-regulated murine marrow cells that contain osteoclast precursors. *Bone* 2003;32:581-90.**

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The authors examined the osteoclastogenic potential of murine bone marrow cells that were fractionated according to their expression of the surface antigen CD45R. Osteoclast-like cells (OCL) with many authentic osteoclast characteristics readily formed in purified CD45R⁺ murine bone marrow cell cultures

after treatment with receptor activator of nuclear factor kappa B ligand (RANKL) and M-CSF. Ovariectomy (Ovx) caused a 1.5- to 2-fold increase in OCL number in unfractionated and CD45R⁺ murine bone marrow cell cultures without affecting OCL formation in CD45R⁻ marrow cells. Limiting dilution assays confirmed that Ovx caused an increase in osteoclast precursor cell number in CD45R⁺ but not CD45R⁻ cells. Mice deficient in the type 1 IL-1 receptor (IL-1R1 KO) do not lose bone mass after Ovx. The authors found that unfractionated, CD45R⁺, and CD45R⁻ bone marrow cells from IL-1R1 KO mice showed no increase in OCL formation in vitro after Ovx. In both the wild-type (WT) and the IL-1R1 KO mice Ovx was associated with a 2-fold increase in pre-B-lymphocytes. About 1.3-3.5% of murine marrow cells expressed surface RANK (the receptor for RANKL) while about 11.9-15% of murine bone marrow cells expressed c-Fms (the receptor for M-CSF). There was little effect of Ovx on cells expressing either RANK or c-Fms. These results demonstrate that CD45R expression identifies a subset of murine bone marrow cells whose ability to form OCL in vivo is regulated by estrogen in WT but not IL-1R1 KO cells. The effects of estrogen on bone mass may be related to these responses.

Bogadi-Šare A, Zavalic M, Turk R. Utility of a routine medical surveillance program with benzene exposed workers. Am J Ind Med 2003;44:467-73.

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This study evaluates the utility of routine medical survey applied to benzene-exposed workers by analysing the haematological, immunological, and cytogenetic assay results. The results of a previous study of haematological, immunological, and cytogenetic assays in benzene-exposed workers (up to 15 ppm) are used to discuss medical surveillance program by defining the relationship between various benzene exposure concentrations and toxic endpoints. Exposure to benzene concentration lower than 5 ppm does not produce any abnormal hematological measurements. For benzene cumulative exposure above 100 (ppm-years), some blood indices [mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), band neutrophils] show significant differences in comparison to the control group. The incidence of dicentric chromosomes was higher and the level of B-lymphocytes was lower even with workers exposed to 5 ppm of benzene; correlation with exposure indicators was not found. The results suggest that peripheral blood indices, although not sensitive enough, are still the most suitable parameters in a health surveillance program applied to benzene-exposed workers. B-lymphocytes could be a promising indicator of the benzene-induced damage. Cytogenetic tests did not prove to be suitable. Further investigation of useful screening tests for health surveillance program of benzene-exposed workers is still required.

Turk Z, Šesto M, Skodlar J, Ferenčak G, Pokupeć R, Turk N, Stavljenić-Rukavina A. Products of advanced glycation in

patients with type 2 diabetes and vascular disease. Ann Clin Biochem 2003;40:552-9.

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Non-enzymatic glycation leading to advanced glycation endproduct (AGE) formation is thought to contribute to vascular pathology. In this study, AGEs and anti-AGE antibodies in free and immune complex-bound form were assayed in serum of diabetic (DMCAD) (n=69) and nondiabetic (n=78) patients with coronary artery disease (CAD) and in control subjects (n=47) free from vascular disease. A blocking ELISA was used to test immunoreactivity against AGE epitope(s) and a competitive ELISA was used to measure total AGE content. Anti-AGE immunoreactivity was significantly higher in diabetic than in control subjects (p=0.045). Although a wide range of anti-AGE antibody titres was observed in nondiabetic CAD patients, there was no significant difference from those of control subjects. Both diabetic and nondiabetic CAD patients had a higher concentration of circulating immune complexes containing the AGE moiety as antigen than did control subjects (DMCAD vs. control, p=0.041; CAD vs. control, p=0.047). Study patients showed a positive correlation between serum AGE and AGE-immune complexes (DM, r=0.29, p=0.014; CAD, r=0.26, p=0.019), whereas no such correlation was recorded in controls (r=0.08, p=0.89). In conclusion, this is the first study demonstrating increased AGE-immune complexes in patients with CAD, either with or without diabetes, suggesting that AGE-immune complexes might be involved in the atherosclerotic process, either as the result of it or as part of the pathophysiological process.

Pivac N, Muck-Šeler D, Sagud M, Jakovljević M, Mustapić M, Mihaljević-Peleš A. Long-term sertraline treatment and peripheral biochemical markers in female depressed patients. Prog Neuropsychopharmacol Biol Psychiatry 2003;27:759-65.

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The aim of the study was to determine the effects of 4 and 24 weeks of sertraline selective serotonin reuptake inhibitor-SSRI treatment on platelet 5-HT concentration and platelet MAO activity in depressed patients subdivided according to the treatment response based on the reductions in baseline Montgomery-Asperg Depression Rating Scale (MADRS) scores. Platelet 5-HT concentration was significantly lower in all depressed patients at baseline than in healthy subjects. Among patients, platelet 5-HT concentration or platelet MAO activity did not differ before treatment. There was no significant correlation between MADRS scores and peripheral biochemical markers. The limitation of the study was in a small number of patients, but its advantage was in a long-term (24 weeks) follow-up of both patients and healthy controls. The results of this study show that long-term sertraline treatment induced remission and response in 87% patients, decreased platelet 5-HT concentration after 4 and 24 weeks of treatment and decreased platelet MAO activity after 24 weeks. They also suggest that pretreatment values of platelet 5-HT and platelet MAO might not predict therapeutic outcome to sertraline treatment in female depressed patients.