

**UNIVERZITA KARLOVA V PRAZE,
LÉKAŘSKÁ FAKULTA V HRADCI KRÁLOVÉ
A
FAKULTNÍ NEMOCNICE V HRADCI KRÁLOVÉ**

V. VĚDECKÁ KONFERENCE

P R O G R A M



13. prosince 2000

**Velká posluchárna teoretických ústavů Lékařské fakulty UK,
Šimkova 870, Hradec Králové**

T e c h n i c k é p o k y n y

Vědecká konference je zároveň částí oponentního řízení grantů následujících grantových agentur:

Grantové agentury České republiky
Grantové agentury Univerzity Karlovy
Interní grantové agentury Ministerstva zdravotnictví ČR
Fondu rozvoje vysokých škol
Výzkumných záměrů

V programu jsou uvedeny názvy řešených projektů a jména odpovědných řešitelů.

Ústní sdělení

1. Doba sdělení 10 minut. Diskuse k jednotlivým projektům bude najednou na závěr sekce. Vzhledem k počtu končících grantů je nutno bezpodmínečně dodržet časový limit.
2. K dispozici je projekce diapozitivů 5 x 5 cm, zpětná projekce, video a dataprojekce.
3. Materiály k projekci se předávají nejpozději 15 minut před začátkem sekce v místnosti č. 14 vedle velké posluchárny.

Plakátová sdělení

Postery budou vyvěšeny po celou dobu konání konference. Prohlídka plakátových sdělení je možná v průběhu přestávek.

Po tuto dobu bude u panelu přítomen řešitel nebo spoluřešitel projektu.

Středa 13. 12. 2000

- 8.00 - 8.10 **Z a h á j e n í k o n f e r e n c e**
prof. MUDr. Ivo Šteiner, CSc., děkan lékařské fakulty
doc. MUDr. Leoš Heger, CSc., ředitel fakultní nemocnice
- Sekce I** **Předsedající: doc. MUDr. Vladimír Geršl, CSc.**
- 8.10 - 8.20 Simulace dentoalveolárních zákroků na výukových modelech
MUDr. Věra Bartáková, CSc.
FRVŠ 1857 (LF)
- 8.20 - 8.30 Začlenění praktické gnatologie do klinické výuky protetické
stomatologie
doc. MUDr. Jiří Bittner, CSc.
FRVŠ 1851 (LF)
- 8.30 - 8.40 Inovace preklinické výuky stomatologie v modernizované fantomové
laboratoři
doc. MUDr. Věra Hubková, CSc.
FRVŠ 1849 (LF)
- 8.40 - 8.50 Začlenění dentální implantologie do výuky stomatologie na lékařských
fakultách
MUDr. Dana Kopecká
FRVŠ 1858 (LF)
- 8.50 - 9.00 Soubor výukových programů pro výuku statistiky na lékařských
fakultách
Mgr. Iva Krulichová
FRVŠ 1852 (LF)
- 9.00 - 9.10 Digitalizace dokumentačních prací pro topografické pitvy a přednášky
z anatomie
MUDr. Olga Rejtarová
FRVŠ 1848 (LF)
- 9.10 - 9.20 Inovace teoretické a praktické přípravy studentů v dětské stomatologii
MUDr. Lucie Strnadová
FRVŠ 1861 (LF)
- 9.20 - 9.30 Zavedení digitálně řízené bicyklové ergometrie v praktické výuce
fyziologie
MUDr. Václav Šafka
FRVŠ 1854 (LF)

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- 9.30 - 9.40 Výuka základů gnatologie v rámci preklinické stomatologie
MUDr. Dagmar Vahalová
FRVŠ 1853 (LF)
- 9.40 - 9.55 DISKUSE K VÝŠE UVEDENÝM PROJEKTŮM
- 9.55 - 10.10 *Přestávka - občerstvení, prohlídka plakátových sdělení*
- Sekce II** **Předsedající: prof. MUDr. Zbyněk Hrnčíř, DrSc.**
- 10.10 - 10.20 Metabolismus proteinů a aminokyselin s rozvětveným řetězcem u renální insuficience – terapeutické možnosti
doc. MUDr. Milan Holeček, CSc.
GA ČR 306/98/0046 (LF)
- 10.20 - 10.30 Enkapsulace savčích nervových buněk pro léčbu neurodegenerativních onemocnění
(odp. řešitel: Ing. Jaromír Lukáš, CSc., AV ČR, Praha)
doc. MUDr. Jaroslav Mokrý, Ph.D.
GA ČR 304/98/0267 (LF)
- 10.30 - 10.40 Závažná orgánová selhání: experimentální a klinické aspekty, možnosti prevence a terapeutického ovlivnění
koordinátor: **prof. MUDr. RNDr. Miroslav Červinka, CSc.**
MSM 111500001 (LF)
- 10.40 - 10.50 Hepatologie - fyziologické, patofyziologické a klinické aspekty
koordinátorka: **doc. MUDr. Zuzana Červinková, CSc.**
MSM 111500003 (LF)
- 10.50 - 11.00 Patogeneze, diagnostika a terapie nádorových onemocnění
koordinátor: **prof. MUDr. Jaroslav Malý, CSc.**
MSM 111500002 (LF)
- 11.00 - 11.10 Inovace lékařského kurikula (s ohledem na vstup do Evropské unie).
koordinátor: **prof. PhDr. Jiří Mareš, CSc.**
MSM 111500005 (LF)
- 11.10 - 11.20 Vývoj softwarových prostředků pro práci s medicínskými informacemi, pro zpracování biosignálů, pro podporu rozhodování lékaře a pro zvýšení kvality vzdělávání
koordinátor: **prof. MUDr. Pravoslav Stránský, CSc.**
MSM 111500004 (LF)
- 11.20 - 11.35 DISKUSE K VÝŠE UVEDENÝM VÝZKUMNÝM ZÁMĚRŮM
- 11.35 - 12.20 *Přestávka na oběd*

Vědecká konference LF UK a FN v Hradci Králové, 13. prosince 2000

- Sekce III** **Předsedající: prof. MUDr. Pavel Rozsival, CSc.**
- 12.20 - 12.30 Časná predikce kardiotoxicity antineoplastických látek
MUDr. Michaela Adamcová, CSc.
GA UK 272/98 (LF)
- 12.30 - 12.40 Studium dynamiky změn buněčných membrán po působení
modelových xenobiotik na buňky pěstované in vitro
prof. MUDr. RNDr. Miroslav Červinka, CSc.
GA UK 274/98 (LF)
- 12.40 - 12.50 Metabolismus proteinů u jaterního poškození a možnosti ovlivnění
reparace jater zásahem do metabolismu aminokyselin
doc. MUDr. Milan Holeček, CSc.
GA UK 276/98 (LF)
- 12.50 - 13.00 Účinky kortikoliberinu na sekreci adenohipofyzárních hormonů.
Farmakologické ovlivnění nádorů hypofýzy induktory apoptózy in
vitro
MUDr. Martina Mareková
GA UK 279/98 (LF)
- 13.00 - 13.10 Analýza výsledků operací katarakt
doc. MUDr. Jan Novák, CSc.
GA UK 283/98 (LF)
- 13.10 - 13.20 Studie molekulárních mechanismů aterogeneze u familiární
hyperlipidémie
doc. MUDr. Vladimír Bláha, CSc.
IGA MZ ČR NB/4548-3/98 (FN)
- 13.20 - 13.30 Klinické a biologické aspekty řízené tkáňové regenerace ve
stomatologii
doc. MUDr. Ivo Dřížhal, CSc.
IGA MZ ČR NK/4802-3/98 (LF)
- 13.30 - 13.40 Diagnostika vezikoureterálního refluxu pomocí kontrastní
ultrazvukové cystografie
doc. MUDr. Pavel Eliáš, CSc.
IGA MZ ČR NE/4688-3/98 (LF)
- 13.40 - 13.55 DISKUSE K VÝŠE UVEDENÝM PROJEKTŮM
- 13.55 - 14.10 *P ř e s t á v k a - občerstvení, prohlídka plakátových sdělení*

Vědecká konference LF UK a FN v Hradci Králové, 13. prosince 2000

Sekce IV

Předsedající: doc. RNDr. Jan Krejsek, CSc.

- 14.10 - 14.20 Kontaktní fotoalergie jako příčina některých dermatóz
MUDr. Karel Ettler, CSc.
IGA MZ ČR NK/4689-3/98 (LF)
- 14.20 - 14.30 Dlouhodobý vliv hemodialýzy a peritoneální dialýzy na imunitu
nemocných s chronickým selháním ledvin
MUDr. Petr Fixa, CSc.
IGA MZ ČR NK/4565-3/98 (FN)
- 14.30 - 14.40 Změny vybraných hormonálních a metabolických ukazatelů při
přechodu z parenterální na enterální výživu
MUDr. Eduard Havel
IGA MZ ČR NB/4788-3/98 (LF)
- 14.40 - 14.50 Peroperační radioimunologická detekce kolorektálního karcinomu
MUDr. Pavel Hladík
IGA MZ ČR NC/4532-3/98 (FN)
- 14.50 - 15.00 Konfigurace imunoblotu jako konfirmační sérologické metody
v diagnostice Lymeské boreliózy
MUDr. Karel Honegr
IGA MZ ČR NI/4549-3/98 (FN)
- 15.00 - 15.10 Hemodynamické, klinické a biochemické sledování nemocných před a
po transjugulárním intrahepatálním portosystémovém zkratu (TIPS)
část II.
doc. MUDr. Petr Hůlek, CSc.
IGA MZ ČR NA/4558-3/98 (FN)
- 15.10 - 15.20 Střevní propustnost u nespecifických střevních zánětů - úloha
v patogenezi a monitoraci průběhu a léčby
MUDr. Pavel Kohout
IGA MZ ČR NB/4529-3/98 (FN)
- 15.20 - 15.35 DISKUSE K VÝŠE UVEDENÝM PROJEKTŮM
- 15.35 - 15.50 ***P ř e s t á v k a - občerstvení, prohlídka plakátových sdělení***

- Sekce V** **Předsedající: prof. MUDr. Zbyněk Vobořil, DrSc.**
- 15.50 - 16.00 Bezpečnost a efektivita kysličníku uhličitého jako intravaskulární
kontrastní látky
doc. MUDr. Antonín Krajina, CSc.
IGA MZ ČR NA/4545-3/98 (FN)
- 16.00 - 16.10 Mnohočetná rezistence leukemických buněk vůči působení cytostatik
a její průkaz in vitro
doc. RNDr. Jan Krejsek, CSc.
IGA MZ ČR NM/20-3/98 (LF)
- 16.10 - 16.20 Elektrofyziologická diagnostika neuropsychiatrických poruch
a objektivizace výsledků jejich terapie
doc. MUDr. Miroslav Kuba, CSc.
IGA MZ ČR NF/4800-3/98 (LF)
- 16.20 - 16.30 Detekce reziduální choroby mnohočetného myelomu po
vysokodávkové chemoterapii
MUDr. Vladimír Maisnar
IGA MZ ČR NC/4535-3/98 (FN)
- 16.30 - 16.40 Adoptivní imunoterapie jako součást kombinované léčby
metastatického postižení jater
MUDr. Bohuslav Melichar, Ph.D.
IGA MZ ČR NI/4676-3/98 (LF)
- 16.40 - 16.50 Fonochirurgická léčba hlasových poruch
MUDr. Ivana Nováková
IGA MZ ČR NK/4528-3/98 (FN)
- 16.50 - 17.00 Elektronické kompendium laboratorní medicíny
doc. MUDr. Vladimír Palička, CSc.
IGA MZ ČR NO/4692-3/98 (LF)
- 17.00 - 17.15 DISKUSE K VÝŠE UVEDENÝM PROJEKTŮM
- 17.15 - 17.30 *P ř e s t á v k a - občerstvení, prohlídka plakátových sdělení*

- Sekce VI** **Předsedající: doc. MUDr. Zuzana Červinková, CSc.**
- 17.30 - 17.40 Vztah kapilární neovaskularizace k metastatické potenci a prognóze u karcinomu prsu
MUDr. Aleš Ryška
IGA MZ ČR NC/4559-3/98 (FN)
- 17.40 - 17.50 Prognostický význam biochemického monitorování v gerontologii
RNDr. Dagmar Solichová
IGA MZ ČR NG/1-3/98 (FN)
- 17.50 - 18.00 Elektrofyzilogie zrakových funkcí u diabetiků
prof. MUDr. Jaromír Svěrák, DrSc.
IGA MZ ČR NK/4564-3/98 (FN)
- 18.00 - 18.10 Klinická analýza oseointegrovaných dentálních implantátů z hlediska povrchové úpravy fixtur
doc. MUDr. Antonín Šimůnek, CSc.
IGA MZ ČR NK/4789-3/98 (LF)
- 18.10 - 18.20 Intenzivní cyklická chemoterapie s podporou plnou krví bohatou na progenitorové buňky /PBPC/ v léčbě karcinomu prsu a plic
MUDr. Jaroslav Vaňásek, CSc.
IGA MZ ČR NC/4569-3/98 (FN)
- 18.20 - 18.30 Antioxidační ochranný systém u pacientů s dyslipoproteinémií
Ing. Jaroslava Vávrová
IGA MZ ČR NB/4540-3/98 (FN)
- 18.30 - 18.40 Přínos barevné duplexní ultrasonografie v diagnostice ischemické choroby dolních končetin.
MUDr. Petr Vodňanský
IGA MZ ČR NA/4560-3/98 (FN)
- 18.40 - 18.55 DISKUSE K VÝŠE UVEDENÝM PROJEKTŮM
- 18.55 **U k o n ě n í k o n f e r e n c e**
prof. MUDr. RNDr. Miroslav Červinka, CSc.,
proděkan lékařské fakulty pro vědu a výzkum

**VÝZKUMNÉ ZÁMĚRY A PROJEKTY PREZENTOVANÉ FORMOU
PLAKÁTOVÝCH SDĚLENÍ**

1. Závažná orgánová selhání: experimentální a klinické aspekty, možnosti prevence a terapeutického ovlivnění
koordinátor: **prof. MUDr. RNDr. Miroslav Červinka, CSc.**
MSM 111500001 (LF)
2. Hepatologie - fyziologické, patofyziologické a klinické aspekty
koordinátor: **doc. MUDr. Zuzana Červinková, CSc.**
Výzkumný záměr MSM 111500003 (LF)
3. Patogeneze, diagnostika a terapie nádorových onemocnění
koordinátor: **prof. MUDr. Jaroslav Malý, CSc.**
Výzkumný záměr MSM 111500002 (LF)
4. Vývoj softwarových prostředků pro práci s medicínskými informacemi, pro zpracování biosignálů, pro podporu rozhodování lékaře a pro zvýšení kvality vzdělávání
koordinátor: **prof. MUDr. Pravoslav Stránský, CSc.**
MSM 111500004 (LF)
5. Chronická gastritida indukovaná infekcí *Helicobacter pylori* a autoimunitními mechanismy – zdroj dyspeptických obtíží?
prof. MUDr. Bohumil Fixa, DrSc.
IGA MZ ČR NK/6174-2/00 (LF)
6. Nové látky chelatující železo – problematika jejich kardiovaskulárních, potenciálně kardioprotektivních a biotransformačních účinků
doc. MUDr. Vladimír Geršl, CSc.
GA ČR 305/00/0365 (LF)
7. Bezpečnost a efektivita kysličníku uhličitého jako intravaskulární kontrastní látky
doc. MUDr. Antonín Krajina, CSc.
IGA MZ ČR NA/4545-3/98 (FN)
8. Interakce 7-methoxytacrinu a gelanthaminu s vybranými neuroprotektivy
doc. MUDr. Vladimír Palička, CSc.
IGA MZ ČR NL/6091-3/00 (FN)

9. Rekonstrukce kloubních povrchů použitím autologních osteochondrálních štěpů, autologních kultur chondrocytů v suspenzi a na bioaktivním sklokeramickém nosiči. Experimentální klinická studie.

MUDr. Jaroslav Pavlata

IGA MZ ČR ND/6042-3/00 (FN)

10. Možnost ovlivnění restenosis implantací radioaktivních stentů s velmi nízkou, cyklotronem navozenou aktivitou

MUDr. Josef Štásek, Ph.D.

IGA MZ ČR NA/4786-3/98 (LF)

11. Standardizace vyšetřovacích metod na stabilografické plošině za účelem objektivizace změn pohybového ústrojí

MUDr. Vlasta Tošnerová, CSc.

IGA MZ ČR NK/6078-3/00 (LF)

**NA LF UK A FN V HRADCI KRÁLOVÉ SE V ROCE 2000 DÁLE ŘEŠILY
NÁSLEDUJÍCÍ PROJEKTY**

(abecedně podle jmen řešitelů)

V tomto přehledu nejsou uvedeny všechny smluvně podložené spolupráce na projektech, jejichž odpovědní řešitelé jsou z jiných organizací než z LF UK a FN v Hradci Králové.

1. Troponin u dětí s vrozenými srdečními vadami
MUDr. Michaela Adamcová, CSc.
GA ČR 305/98/P261 (LF)
2. Úloha fenotypu a genotypu familiární hyperlipoproteinémie v procesu aterogeneze u ischemické choroby srdeční
doc. MUDr. Vladimír Bláha, CSc.
IGA MZ ČR NB/5205-3/99 (FN)
3. Porovnání výskytu neurovaskulárních kompresí v oblasti rostrální ventrolaterální medully u hypertoniků a normotoniků. Prospektivní MR studie.
MUDr. Jiří Ceral, Ph.D.
IGA MZ ČR NA/6169-3/00 (LF)
4. Adenomy hypofýzy kultivované in vitro: vliv somatostatinových analogů a induktorů apoptózy
MUDr. Jan Čáp, CSc.
IGA MZ ČR NB/6172-3/00 (LF)
5. Testování střevní propustnosti při modelovém poškození střeva a jater
doc. MUDr. Zuzana Červinková, CSc.
GA UK 1/99 (LF)
6. Farmakokinetika nízkodávkovaného metotrexátu u pacientů s psoriázou, podaného v časných stádiích onemocnění
MUDr. Jiří Grim
GA UK 9/99 (LF)
7. Přínos stanovení dipeptidylpeptidázy IV (DPP IV) v diferenciální diagnostice tumorů štítné žlázy
MUDr. Ivana Kholová
GA UK 87/00 (LF)

8. Electrophysiological Assessment of Human Cognitive Processes
doc. MUDr. Miroslav Kuba, CSc.
Společný výzkumný projekt s Fyziologickými laboratořemi Univerzity v Oxfordu (contractor - Prof. Colin Blakemore): Grant James S. McDonnell Foundation for Cognitive Neurosciences - USA
99-57EE-GLO.04
9. Význam efektivní atriální kontrakce pro sekvenční stimulaci
prof. MUDr. Jiří Kvasnička, CSc.
IGA MZ ČR NA/5403-3/99 (LF)
10. Vliv transparence nitrooční čočky na rozlišovací schopnost oka
MUDr. Hana Langrová, Ph.D.
GA ČR 309/00/D056 (LF)
11. Vztah bilance tekutin k neuromuskulárním poruchám u kriticky nemocných
MUDr. Jan Maňák
IGA MZ ČR NB/5197-3/99 (FN)
12. Populační modelování farmakokinetiky a farmakodynamiky v klinické farmakologii
prof. MUDr. Jiřina Martínková, CSc.
COST OC B15.10/1999 (LF)
13. Neurální transplantace do experimentálního modelu Huntingtonovy choroby
doc. MUDr. Yvona Mazurová, CSc.
IGA MZ ČR NF/5400-3/99 (LF)
14. Charakteristika diferenciačního potenciálu neurálních kmenových buněk
doc. MUDr. Jaroslav Mokřý, Ph.D.
GA ČR 304/00/0338 (LF)
15. Aktivní formy kyslíku v patogenezi akutní pankreatitidy a možnost ovlivnění antioxidanty
MUDr. František Musil
IGA MZ ČR NB/6043-3/00
16. Kvalita života kriticky nemocných léčených v podmínkách intenzivní a resuscitační péče - prospektivní multicentrická studie
MUDr. Renata Pařízková
IGA MZ ČR NK/4530-3/98 (FN)

17. Aplikace 13C dechových testů do klinické praxe v pediatrii
doc. MUDr. Oldřich Pozler, CSc.
IGA MZ ČR NE/6164-3/00 (LF)
18. Morální názorová kompetence u studentů medicíny, měření a celková analýza
MUDr. Birgita Slováčková
GA UK 296/00 (LF)
19. Vliv poměru arteriální a portální perfúze jater na inzulínovou rezistenci a jaterní funkce při jaterní cirhóze
MUDr. Václav Šafka, Ph.D.
GA ČR 306/99/P014 (LF)
20. Stanovení funkční aktivity a fenotypu tumor infiltrujících lymfocytů u nemocných s ovariálními tumory
Mgr. Miroslava Toušková
IGA MZ ČR NH/5196-3/99 (FN)
21. Změny metabolismu lipidů a jejich mediátorových účinků u pacientů s kolorektálním karcinomem - perspektivní využití v nutriční podpoře
prof. MUDr. Zdeněk Zadák, CSc.
IGA MZ ČR NC/6171-3/00 (LF)
22. Analýza vydechovaných plynů pro sledování metabolických poruch a účinků nutričních substrátů pomocí GC/MS systému
(odp. řešitel: prof. Ing. Jiří Gasparič, DrSc., Univerzita Karlova v Praze, Farmaceutická fakulta v Hradci Králové)
prof. MUDr. Zdeněk Zadák, CSc.
GA ČR 203/99/1165 (LF)
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**SOUHRNY VÝZKUMNÝCH ÚKOLŮ
ŘEŠENÝCH NA LF UK A FN V HRADCI KRÁLOVÉ
(ABECEDNĚ)**

Title of the research project: Troponin u dětí s vrozenými srdečními vadami (Troponin in children with congenital heart diseases)	
Grant Agency: Czech Republic	Project Number: P261
Principal Researcher: Michaela Adamcová	
Joint Researchers: Václav Pelouch, Zuzana Červinková, Jan Škovránek	
Starting date: 1.9.1998	Duration (years): 3
Funds allocated for project - total in Czech crowns: 220000	
Summary of 2000 results	
Title of the presentation: Isolation of cardiac troponin T in human atrial and ventricular musculature	
Authors: Michaela Adamcová (1), Václav Pelouch (2) Dept. Physiology, Charles University in Prague, Faculty of Medicine in Hradec Králové (1), Dept. Medical Chemistry and Biochemistry, Charles University, 2nd Faculty of Medicine in Prague (2)	
<p>The structure of ventricles and atria of the mammalian myocardium differs considerably. The aim of our study was to determine the changes of the regulatory protein troponin T in myocardial samples obtained during surgical intervention from children (age 8.2 +/- 1.8 years) operated for different types of congenital heart diseases (tetralogy of Fallot, ventricular and atrial septal defects). The both cytosolic and myofibrillar fractions of cardiac troponin T (cTnT) were isolated by stepwise extraction (Bleier et al. 1998) from the both right ventricular and right atrial musculature. The concentration of proteins was measured using Coomassie Plus Protein Reagent Kit (Pierce). After isolation, one-dimensional SDS polyacrylamide gel electrophoresis was carried out according to a modified version of the method of Laemmli (1970), using a 12% separating gel and a 4% stacking gel. In some cases after SDS-PAGE, proteins were electroblotted onto nitrocellulose membrane for immunoblotting.</p> <p>The ratio of cytosolic and myofibrillar proteins was 0.78 for normoxaemic right ventricles, resp. 0.71 for hypoxaemic right ventricles but 0.95 for normoxaemic right atria, resp. 0.97 for hypoxaemic right atria. The arterial oxygen saturation was 95.5 +/- 0.7 % in normoxaemic patients, resp. 76.9 +/- 2.1 % in hypoxaemic patients. The cytosolic pool of cTnT (measured by commercial kit Elecsys Troponin T STAT Immunoassay – Roche) represents about 12.5 %, the myofibrillar pool of cTnT was about 87.5%; hypoxaemia did not effect this proportion. It is possible to conclude that: a) the concentration of the cytosolic proteins was higher in the atria and 2) in children with chronic hypoxia the above atrio-ventricular differences persisted. Literature: J. Bleier et al.: Clin. Chem. 44(9), 1912 - 1918, 1998 Project was supported by the grant of GACR 305/98/P261.</p>	
Address for correspondence: M. Adamcová, Dept. Physiology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Republic	

Title of the research project: Časná predikce kardiotoxicity antineoplastických látek
(Early prediction of cardiotoxicity caused by antineoplastic drugs)

Grant Agency: Charles University

Project Number: 272/C

Principal Researcher: Michaela Adamcová

Joint Researchers: Vladimír Geršl, Vladimír Palička, Radomír Hrdina, Jarmila Macháčková, Ludmila Koželuhová, Jiřina Hofmanová, Ivana Altmannová, Kateřina Bekirovová

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 715 000

Summary of 2000 results

Title of the presentation: Changes of cardiac troponin T following repeated i.v. administration of Dimefluron

Authors: Michaela Adamcová (1), Vladimír Geršl (2), Jarmila Macháčková (2), Radomír Hrdina (3), Milan Mělka (4), Yvona Mazurová (5), Vladimír Palička (6), Jaroslava Vávrová (6)

Fac. Med., Charles Univ., Hr. Králové: Dept. Physiology (1), Dept. Pharmacology (2), Dept. Biochemistry (4), Dept. Histology (5), Fac. Pharmacy, Charles Univ., Hr. Králové (3), Institute of Clin. Biochemistry and Diagnosis (6)

Dimefluron (3,9 – dimetoxybenfluoren hydrochloride) is considered to be a new potent antineoplastic drug. The cardiac side-effects of repeated i.v. administration of this agent (once a week, 10 administrations) were followed in two groups of rabbits: 1) Dimefluron (12 mg/kg; n=7), 2) Dimefluron (24 mg/kg; n=6) and were compared with the control group (saline 1 ml/kg; n=6). Cardiac troponin T (cTnT) levels after administration of Dimefluron in both doses were always within the physiological range (lower than 0.1 ug/l) in all of the followed-up intervals. Further, no significant increase in the PEP:LVET index was observed during the whole experiment in both doses of Dimefluron. The initial absolute value was 0.4070 +- 0.0167 in the control and 0.4077 +- 0.0199, resp. 0.4145 +-0.0369 in Dimefluron treated groups. There were no significant differences between the control and Dimefluron treated groups in the left ventricular dP/dt max (1174.38 +- 103.26 kPa/s vs 1336.98 +- 149.81 kPa/s resp. 1438.17 +- 128.02) at the end of experiment. Lack of cardiotoxicity of the new drug under study were also supported by no premature death of animals and histological examination. Normal appearance of the tissue prevail; the changes of tinction (increased eosinophilia of the cytoplasm of some cardiocytes) and isolated cells with degenerated myofibrils were similar to the control group. It is possible to conclude, that no significant deterioration of the examined parameters was found during repeated i.v. administration of Dimefluron which is important from possible clinical use of this new antineoplastic agent. Project was supported by the Charles University Grant Agency, No. 272/1998C and Research Project CEZ:J13/98:111500002.

Address for correspondence: M. Adamcová, Dept. Physiology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Simulation of dentoalveolar procedures on teaching models

Grant Agency: Ministry of Education

Project Number: 1857/2000

Principal Researcher: Věra Bartáková

Joint Researchers: Štefan Nátek

Starting date: 1.1. 2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 170000

Summary of 2000 results

Title of the presentation: Simulation of dentoalveolar procedures on teaching models

Authors: Věra Bartáková, Štefan Nátek

Fac. Med., Charles Univ., Hr. Králové: Dept. of Dentistry

The main purpose of the project is to provide students of stomatology with better training for everyday practice. The simulated dentoalveolar operations lead students step by step to manage the operating technique. Students have the opportunity to stop at any moment to consult the course of action. The procedure looks like real from the very beginning. Students wear the operating grows, masks, caps and gloves. They follow the aseptic rules. To perform the procedure they also prepare the instruments together with the dental drill, a chilling equipment and suction tool. They work in pairs. One of them works as a surgeon, the other one as an assistant. They take turns after a procedure.

It is possible to perform five dentoalveolar operations on each of the teaching models:

- Impacted mandibular third molar extraction
- Impacted maxillary canine extraction
- Apicectomy 3x

Students work in peace, without stress and they can fully concentrate on the technique of a procedure. It highly improves their skills and confidence while treating a real patient. Safety is what matters.

If students are not sure about their skills, they can repeat operation several times to master the technique.

The simulation system ranks among the latest trends in training of medical students to improve their quality.

For training purpose we used teaching models made by a FRASACO company. After reshaping, those models are ready to use for further training.

Literature: Thomson-PJ et al.: Dent-Update 23(7), 283-286, 1996

Project was supported by the Ministry of Education Grant Agency, No 1857/2000.

Address for correspondence: V. Bartáková, Dept. of Dentistry, Faculty Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Study of molecular mechanisms of atherogenesis in familiar hyperlipidaemia

Grant Agency: Ministry of Health

Project Number: NB/4548-3

Principal Researcher: doc.MUDr.Vladimír Bláha, CSc.

Joint Researchers: MUDr. Eduard Havel, RNDr. Dagmar Solichová, MUDr. Radomír Hyšpler, prof. MUDr. Milan Bláha, CSc., prof. MUDr. Zdeněk Zadák, CSc.
Faculty Hospital, Charles University, Dept. Gerontology and Metabolic Care, Hradec Králové, Czech Republic

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2500000

Summary of 2000 results

Title of the presentation: Effect of low-density lipoprotein apheresis on fatty acid and lipoprotein metabolism

Authors: Vladimír Bláha (1), Eduard Havel (1), Dagmar Solichová (1), Radomír Hyšpler (1), Milan Bláha (2), Zdeněk Zadák (1). Faculty Hospital Charles University, Department of Gerontology and Metabolic Care (1), Department of Haematology (2), Hradec Králové, Czech Republic.

The aim of this study was to analyze lipid metabolism in 5 hyperlipidaemic subjects (3 man, 2 woman, age 17-55y) undergoing aggressive hypolipidaemic therapy using LDL-immunoapheresis. Blood samples were drawn four times every three months before each LDL-apheresis in Expt. 1, and/or immediately after LDL-apheresis in Expt. 2 and analysed using capillary gas chromatography, reversed phase high-performance liquid chromatography, spectrofluorometry and spectrophotometry. Results: In Expt. 1 vitamin E in serum and lipoprotein fractions, neither serum TBARS did change significantly. Plasma phospholipids significantly decreased. Red blood cell membrane (RBCM) phospholipids, SUFA, MUFA and PUFA did not change significantly. Plasma linoleic acid initially significantly increased. LDL-bound gamma-linolenic acid did not change significantly, but correlated with TAG. Plasma docosahexaenoic PUFA did not change significantly. Plasma arachidonic acid initially nonsignificantly increased. Other plasma fatty acids did not differ significantly. After LDL-apheresis in Expt. 2, we observed significantly decreased serum TBARS and significantly decreased serum total vitamin A and E and vitamin E in lipoprotein fractions. Lipoprotein myristic acid was significantly increased in IDL and marginally in LDL, and was decreased in HDL. Lipoprotein stearic acid was non-significantly increased in LDL and VLDL. Linoleic acid was significantly increased in plasma, but decreased in LDL. Arachidonic acid non significantly decreased. Docosahexaenoic acid significantly decreased in plasma, and non-significant increased in LDL. WE CONCLUDE that LDL-apheresis not only decreases the pool of atherogenic LDL, but it also induces other antiatherogenic properties via decreased lipoperoxidation, which might be a consequence of a short-term changes in the fatty acids composition.

Address for correspondence: V. Bláha, Department of Gerontology and Metabolic Care, Faculty Hospital, Charles University, Sokolská 581, 50005 Hradec Králové, Czech Republic

Title of the research project: The role of phenotype and genotype of familial hyperlipoproteinemia in atherogenesis of coronary artery disease

Grant Agency: Ministry of Health

Project Number: NB/5205-3

Principal Researcher: doc.MUDr.Vladimír Bláha, CSc.

Joint Researchers: MUDr. Pavel Vyroubal, RNDr. Dagmar Solichová, MUDr. Radomír Hyšpler, RNDr. Martin Beránek, CSc., prof. MUDr. Zdeněk Zadák, CSc., MUDr. Dušan Černohorský

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2500000

Summary of 2000 results

Title of the presentation: Coronary atherosclerosis associates with metabolism of saturated and polyunsaturated fatty acids

Authors: Vladimír Bláha (1), Pavel Vyroubal (1), Dagmar Solichová (1), Radomír Hyšpler (1), Dušan Černohorský (1), Zdeněk Zadák (1), Martin Beránek (2)
Faculty Hospital, Charles Univ., Dept.Gerontol.Metabol.Care (1), Dept. Biochem. (2)

The role of individual fatty acids of serum, lipoprotein fractions and erythrocyte membrane in coronary artery disease (CAD) has been studied in patients who underwent an elective coronary angiography for CAD (n=59, age 33-73 years) in Group A (luminal narrowing <50%) and Group B (>50% stenosis). Hyperlipidaemia was treated conventionally using statins, resins and/or fibrates in standard doses. Patients were counseled to follow diet which limits dietary cholesterol to <300mg/day, saturated fats <10% of total calories, and total fats to <30% of total calories. Exclusion criteria were: acute myocardial infarction within three months of blood sampling, obesity (body mass index over 30), thyreopathy (i.e. hyper- or hypothyreosis), treatment with thiazide diuretics or steroid hormones (incl. hormonal replacement therapy during menopause), alcoholism, and diabetes mellitus treated by insulin. Capillary gas chromatography was used for determination of fatty acids. Retinol and alpha-tocopherol were analyzed by reversed-phase high-performance liquid chromatography, other parameters were determined spectrofluorometrically and spectrophotometrically. Severe CAD in Group B significantly correlated with higher age, serum LDL/HDL cholesterol ratio, plasma C18:3n6, IDL C18:1n7, HDL C22:6n3, and erythrocyte membrane C22:6n3 (p<0.05). IDL C18:1n7 was significantly higher in Group A (p<0.05). Plasma C18:3n6, HDL C22:6n3, and erythrocyte membrane C22:6n3 fatty acids were significantly higher in Group B (p<0.05). We conclude that an altered metabolism of gamma-linolenic (C18:3n6) and docosahexaenoic (C22:6n3) fatty acids associates with coronary atherosclerosis, indicating enhanced transport of plasma C18:3n6 and removal of HDL C22:6n3 from arterial wall cells.

Address for correspondence: V. Bláha, Department of Gerontology and Metabolic Care, Faculty Hospital, Charles University, Sokolská 581, 50005 Hradec Králové, Czech Republic

Title of the research project: Pituitary adenomas in tissue culture: The influence of somatostatin analogues and inductors of apoptosis.

Grant Agency: Ministry of Health

Project Number: NB/6172-3

Principal Researcher: Jan Čáp

Joint Researchers: Viktor Bartanusz, Vladimír Beneš, Jaroslav Cerman, Josef Marek, Martina Mareková, Jiří Náhlovský, Stanislav Němeček, Miroslav Solař, Hana Straková, Petr Šuba

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 598000 (y. 2000)

Summary of 2000 results

Title of the presentation: The influence of somatostatine analogues with various receptor specificity on homonal secretion of acromegalic adenomas in vitro. A pilot study.

Authors: Jan Čáp (1), Miroslav Solař (1), Martina Mareková (2), Jaroslav Cerman (2), Jiří Náhlovský (3), Petr Šuba (2), Stanislav Němeček (3), Vladimír Beneš (4), Josef Marek (5)

Charles Univ., Fac. Med. Hr. Králové: Dept. of Internal Medicine (1), Dept. of Medical Biochemistry (2), Dept. of Neurosurgery (3). 1st Fac. Med. Prague: Dept. Neurosurgery (4), 3rd Med. Dept. (5)

Somatostatin (SS) exerts its biological effects via five distinct high affinity membrane receptor (SSTR) subtypes. Human GH-secreting adenomas appear to variably express the different SSTR subtypes. Recent studies using SS analogues that are preferential for the human SSTR2 and SSTR5 receptor subtypes, such as BIM-23197 and BIM-23268, respectively, suggest the involvement of both SSTR2 and SSTR5 in regulating GH secretion from somatotroph adenomas. The aim of our study is to address the question whether combinations of analogues preferentially binding these two receptors are more potent in inhibition of hormonal secretion.

Ten GH-secreting adenomas were cultivated in vitro. After two days in culture the influence of following substances (in concentrations of 50 and 100 nmol/l in defined medium, incubation for three hours) on GH secretion was tested: a) cyclic somatostatin 14 (binds all SSTR subtypes) b) BIM 23014 (lanreotid, preferentially binds SSTR2) c) BIM 23197 (preferentially binds SSTR2) d) BIM 23268 (preferentially binds SSTR5) e) combination BIM 23014 + BIM 23268 f) combination BIM 23197 + BIM 23268.

The decrease in GH secretion was similar for all somatostatins used (including the SSTR5 preferentially binding BIM 23268). We were unable to demonstrate any amplification effect of the combination of SSTR2 and SSTR5 preferentially binding SS analogues at least in the concentrations used. Whether the same is true for lower (submaximal) concentrations will be the subject of further study.

The project was supported by the Czech Ministry of Health Grant Agency, No NB/6172-3.

Address for correspondence: J. Čáp, Second Dept. of Internal Medicine, University Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Neurovascular compression of the rostral ventrolateral medulla in patients with essential hypertension compared to normotensive subjects. Prospective MR study.

Grant Agency: Ministry of Health

Project Number: NA/6169-3

Principal Researcher: Jiří Ceral

Joint Researchers: Jan Žižka, Jiří Kvasnička, Pavel Eliáš

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1129000

Summary of 2000 results

Title of the presentation: Neurovascular compression of the rostral ventrolateral medulla in hypertensive patients compared to normotensive subjects - first results.

Authors: Jiří Ceral (1), Jan Žižka (2), Jiří Kvasnička (1), Pavel Eliáš (2)

Fac. Med. Charles Univ., Hr. Králové: Dept. of Internal Medicine (1), Dept. of Radiology (2)

Rostral ventrolateral medulla oblongata (RVLM) is a key part of the central nervous system for regulation of blood pressure. Compression of the left RVLM by an abnormally located artery may be one of the possible causes of essential hypertension as some experimental studies, postmortem and neurosurgical observations suggest. Only recently studies of two small series of patients operated on with good effect for hypertension exclusively were published. Why is right-sided compression less frequent and what is its relation to hypertension is not clear. A prerequisite for the optimal choice of patients suitable for surgical solution is an adequate scan of the incriminated area. The only suitable method is a magnetic resonance (MR). Published MR studies have very different results mainly due to methodological problems. Our small pilot study seemed to be in agreement with the assumption of a higher rate of neurovascular compressions at the left RVLM in hypertensive patients. In order to prove such an assumption we started a prospective blind study using the combination of 2 D MR imaging and MR angiography on patients with essential hypertension and normotensive subjects. We found significantly higher rate of compressions of the medulla oblongata on the left side compared to the right one. Left-sided compressions located precisely at the area of the RVLM seem to be not so frequent as in some previously published studies.

Project is supported by the Ministry of Health Grant Agency, No NA/6169-3

Address for correspondence: J. Ceral, Dept. of Internal Medicine, Charles University Faculty of Medicine

Title of the research project: Modernisation of the laboratory for practical training in cytology of cells cultivated in vitro

Grant Agency: Ministry of Education

Project Number: 1287/1999

Principal Researcher: doc. MUDr. RNDr. Miroslav Červinka, CSc.

Joint Researchers: MUDr. Jan Pechl, MUDr. Jana Kolářová, CSc, Mgr. Emil Rudolf

Starting date: 1.1.1999

Duration (years): 1

Funds allocated for project - total in Czech crowns: 1959000

Summary of 1999 results

Title of the presentation: Cytology of living in vitro cultivated cells during practical classes

Authors: Miroslav Červinka, Jan Pechl, Emil Rudolf, Jana Kolařová

Fac. Med., Charles Univ., Hr. Králové: Dept. Medical Biology and Genetics,

This project is a part of our long lasting endeavour to improve the quality of practical classes in medical biology and genetics. In the past we focused on the development of laboratory facilities for molecular biology. This year we aimed our effort to the modern cytology which uses mammalian cells cultivated in vitro.

The majority of financial support (1815000,-Kc) was used for modernisation of a student microscopic laboratory. It includes 35 students microscopes with phase contrast optics, one microscope for teacher, data projector, digital TV camera, digital camera and computer, and biological thermostat. The rest of funding (144000,-Kc) was used for essential reconstruction of electricity in the student laboratory and for necessary consumables and chemicals for practical classes. There was no funding for travel expenses and for personal cost. We were able to completely reconstruct the existing student microscopic laboratory and built the new modern laboratory for microscopy of living cells cultivated in vitro.

These technical improvements enable us to introduce the new practical classes based on observation of living human cells cultivated in vitro. The main advantage is that we bring to the practise the principle of Evidence based medicine. During practical classes each student can perform experiments with cells cultivated in vitro, analyse results and prepare the presentations. The entire learning method is thus oriented to the multimedial applications. Based on the first experience we have prepared new handouts for practical classes and new syllabi for next semester. This new chapter will be included in our new student textbook for practical classes. Students' opinion about this innovation will be evaluated by questionnaire.

The Ministry of Education Grant Agency, No 1287/1999, supported this project.

Address for correspondence: M. Červinka, Dept. of Medical Biology and Genetics, Charles University Faculty of Medicine, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Study of the dynamics of changes in cell membranes after the treatment with model xenobiotics in cells cultivated in vitro

Grant Agency: Charles University

Project Number: 274/98

Principal Researcher: Miroslav Červinka

Joint Researchers: Jan Peychl, Emil Rudolf, Zuzana Červinková

Starting date: 30.11.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 782000

Summary of 2000 results

Title of the presentation: Immunocytochemical analysis of the dynamic changes in Hep2 cells during cell death

Authors: Miroslav Červinka (1), Jaroslav Cerman (2), Jan Peychl (1), Emil Rudolf (1), Zuzana Červinková (3)

Cell death continues to be one of the most intensively studied biological phenomena, with many controversial issues remaining at the cytological level. One unsolved question is for instance the role of cytoskeleton in this process. In our study, we compare data obtained by means of time-lapse videomicroscopy with the immunocytochemical findings. As a model drug for induction of apoptosis we used etoposide (Vepesid inj., Bristol Mayers, 10 microg/ml). As a cell model, stabilised cell line Hep2 grown in the DMEM and cell line HL-60 maintained in RPMI with 10% foetal calf serum were used.

Recently, it has been published that activation of caspase 3 results in specific fragmentation of the cytokeratin 18 (CK18). We monitored this process by immunocytochemical detection of specific caspase-cleaved epitope of the CK18 by monoclonal antibody M30 (Roche) and by detection of activated (cleaved) form of caspase 3 using monospecific antiserum (N. E. Biolabs). Dynamics of membrane changes of living cells was observed during the first 24 hours after the treatment in phase contrast (Olympus inverted microscope IMT 2), TV camera Mitsubishi and recorded by time-lapse video-recorder Mitsubishi (HS-S5600E).

Our results demonstrate that cell membranes movement (blebbing) represents a very characteristic feature of the cell death. We were able to detect caspase specific fragmentation of CK18 already after 6 hours after the beginning of treatment with Etoposide. M30 positivity very closely correlates with the blebbing activity. Detection of activated caspase 3 confirms that intermediate cytokeratin 18 filaments are degraded by caspase 3. Time course of this reaction closely correlates with period of vigorous membrane activity (blebbing).

The Charles University Grant Agency, No 274/98 and Ministry of Education grant No. MSM 111500001 supported this project.

Address for correspondence: M. Červinka, Dept. Med. Biol., Charles University in Prague, Faculty of Medicine of Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Rep.

Title of the research project: Serious organ failures, experimental and clinical aspects, possibilities for prevention and therapeutic management

Grant Agency: Ministry of Education

Project Number: MSM111500001

Principal Researcher: Miroslav Červinka

Joint Researchers: Michaela Adamcová, Jaroslav Cerman, Ivo Dřížhal, Vladimír Geršl, Jiří Horáček, Miroslav Kuba, Yvona Mazurová, Jan Novák, Zbyněk Vobořil, Pavel Živný

Starting date: 1.1.1999

Duration (years): 2

Funds allocated for project - total in Czech crowns: 2875000

Summary of 2000 results

Title of the presentation: Experimental and clinical models for serious organ failures

Authors: M. Červinka (1), M. Adamcová (2), J. Cerman (3), I. Dřížhal (4), V. Geršl (5), J. Horáček (6), M. Kuba (7), Y. Mazurová (8), J. Novák (9), Z. Vobořil (10), P. Živný (11)

Fac. Med., Charles Univ., Hr. Králové, Depts: Med. Biol. (1), Physiol. (2), Med. Biochem. (3), Stomat. (4), Pharmacol. (5), Microbiol. (6), Path. Physiol. (7), Histology (8), Ophthalmol. (9), Surgery (10), Clin. Biochem. (11)

Successful therapeutic management of serious organ failures requires co-operation of several theoretical and clinical departments. Following topics were studied during 2000:

- a) Cardiovascular effects of pyridoxal isonicotinoyl hydrazone (Fe-chelating agent, potentially active in pathological states resulting from both the iron-overload and free radicals formation).
- b) Modulation of differentiation and induction of apoptosis in several in vitro and in vivo models (pituitary adenoma cells, leukemic cell line, epithelial cells). Immunocytochemical techniques were established for detection of specific apoptotic markers.
- c) Reparation of periodontal lesions by guided tissue regeneration.
- d) Development of new electrophysiological methods for early diagnostics of functional disorders of CNS and cognitive functions.
- e) The relation between neurotoxic (ibotenic acid-) lesioned striatum (as a model of neurodegenerative process) and cell proliferation within the subventricular zone of the rat brain.
- f) Incidence of secondary cataract after intraocular lens (IOL) implantation, cellular components on IOL and in humour aqueous.
- g) Implantation of bioactive materials for the treatment of bone defects.
- h) Bacterial complications after organ (renal) and cell (bone marrow) transplantations.
- i) Cytotoxicity and biocompatibility assessment of materials (artificial blood vessels) used in organ failures treatment.
- j) Glucose, urea, lactate and amino acid concentration in skeletal muscle interstitium - a microdialysis study.

Project was supported by the Ministry of Education Research Project, No MSM 111500001.

Address for correspondence: M. Červinka, Dept. Med. Biol., Charles University in Prague,
Faculty of Medicine of Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Rep.

Title of the research project: Testing of intestinal barrier permeability in rats

Grant Agency: Ministry of Education

Project Number: 1524/1999

Principal Researcher: Doc. MUDr. Zuzana Červinková, CSc.

Joint Researchers: MUDr. Jaromír Kočí, Dagmar Radvaková

Starting date: 1.1.1999

Duration (years): 1

Funds allocated for project - total in Czech crowns: 95 000

Summary of 1999 results

Title of the presentation: Testing of intestinal barrier permeability in rat

Authors: Dagmar Radvaková, Jaromír Kočí, Zuzana Červinková

Fac. Med. Charles Univ., Hr. Králové, Dept. Physiology

The intestinal epithelium together with mucus, IgA and gut associated lymphatic tissue provides a barrier against the systemic penetration of antigenic compounds from the gut lumen. Increased permeability has been found in various diseases such as celiac sprue, Crohn's disease, nonsteroidal anti-inflammatory drug-induced enteritis. Intestinal barrier damage can be induced also by ischemic-reperfusion injury of the small bowel in patients after multiple trauma, burn injury, cardiovascular surgery, etc. The main two aims of our study were: a) to introduce model for ischemic-reperfusion injury of small intestine in rat; b) to develop noninvasive method for intestinal permeability evaluation.

Materials and methods: The experiments were performed on male albino Wistar rats with an initial body mass of 220-250 g. Intestinal ischemic-reperfusion injury was induced by occlusion of superior mesenteric artery (SMA) for period of 15, 20 or 30 min. Lactulose-mannitol (LAMA) test was used to measure intestinal permeability 24, 48, 72 h and 7 day after SMA occlusion. The results were compared with those obtained from laparotomized (LAP) rats and intact rats. In the second serie of experiments rats were sacrificed in the above mentioned intervals after SMA occlusion and tissue samples (spleen, liver, and small intestine) were taken for histological evaluation.

Results: 15 min SMA occlusion does not lead to a significant change in intestinal permeability measured by LAMA test 24 h, 72 h and 7 days after gut injury. Significant increase in LAMA test ($p < 0.05$) was found 48 h after SMA occlusion when compered to both LAP and intact rats. These results led us to prolong time of SMA occlusion. Increased DNA synthesis in the intestine 24 h after occlusion documents induction of gut regeneration after ischemic-reperfusion injury.

Address for correspondence: Dagmar Radvaková, Department of Physiology, Faculty of Medicine, Charles University, Šimkova 870, 500 01 Hradec Králové, Czech Republic.

Title of the research project: Testing of intestinal permeability in models of bowel and liver injury

Grant Agency: Charles University

Project Number: 1/99/C

Principal Researcher: Zuzana Červinková

Joint Researchers: Pavel Kohout, Halka Lotková, Dagmar Radvaková, Jaromír Kočí

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 270000

Summary of 2000 results

Title of the presentation: Different models of intestine barrier damage

Authors: Zuzana Červinková, Dagmar Radvaková (1), Halka Lotková (1), Pavel Kohout (2)
Fac. Med. Charles Univ., Hr. Králové: Dept. Physiology (1), Dept. Geront. Metab. (2)

The adult mammalian intestine constitutes a protective barrier against absorption of toxic quantities of bacteria, endotoxin, proteolytic and hydrolytic enzymes and ingested antigens which normally reside in the intestinal lumen. Mucosal integrity and absorption activity could be impaired by various mechanisms. The aim of our study was to introduce different models of intestine injury and to study its impact on the liver. The experiments were performed on male albino Wistar rats with an initial body mass of 220-230 g. Intestinal injury was induced by: a) occlusion of superior mesenteric artery (15 - 30 min) - ischemic-reperfusion injury, b) combination of ischemic-reperfusion injury with partial hepatectomy (67 %), c) administration of indomethacin (2 x 7.5 mg/kg s. c.). Lactulose-mannitol (LAMA) test was used to measure intestinal permeability 24, 48, 72 h and 7 day after intestinal injury. The extent of liver damage and liver regeneration was determined by assessment of serum activity of AST and ALT, liver DNA synthesis, and mitotic activity of hepatocytes in above mentioned intervals after intestinal injury. Enhanced loading of the liver by toxic substances from damaged intestine induced a significant increase of transaminases activity followed by stimulation of liver DNA synthesis. These changes were proportional to the extent of intestine damage. Similar results were obtained in experiment with combined intestine and liver injury. In our experimental design indomethacin administration increased intestinal permeability (LAMA test) but did not lead to increase in transaminases activity and liver DNA synthesis. Protective effect of indomethacin in relation to liver injury was described also in literature (1).

Literature: C. Barriault et al.: Toxicol-Lett., 71, 257-269, 1994

Project was supported by the Charles University Grant Agency, No 1/99/C.

Address for correspondence: Z. Červinková, Dept. of Physiology, Charles Univ. in Prague,
Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech
Republic

Title of the research project: Hepatology - physiological, pathophysiological and clinical aspects

Grant Agency: Ministry of Education

Project Number: MSM 11150003

Principal Researcher: Zuzana Červinková

Joint Researchers: Petr Hůlek, Helena Živná, Jiří Kanta

Starting date: 1.1.1999

Duration (years): 5

Funds allocated for project - total in Czech crowns: 2 495 000

Summary of 2000 results

Title of the presentation: Acute and chronic liver injury in animal experiments and clinical practice

Authors: Zuzana Červinková (1), Petr Hůlek (2), Helena Živná (1), Jiří Kanta (3)
Fac. Med. Charles Univ., Hr. Králové: Dept. Physiology (1), 1st Dept. Internal Med. (2), Dept. Med. Biochem. (3)

The research project is divided into several mutually interconnected branches. Sixteen researchers from seven departments of our faculty participated on the project. Following topics were studied during the last year:

- a) Activation of mitochondrial glycerolphosphate dehydrogenase by triiodothyronine in regenerating rat liver
- b) Influence of t-butylhydroperoxide and carbonylcyanide m-chlorophenyhydrazone on membranes of mitochondria in rat hepatocytes cultivated in vitro
- c) Changes in serum leptin concentration in young rats and in rats after partial hepatectomy.
- d) Influence of high cholesterol diet and pravastatin sodium on the initiation of liver regeneration in rats after partial hepatectomy
- e) Cultivation of stellate cells isolated from normal and fibrotic rat liver, immunocytochemical detection of smooth muscle alpha-actin in cells
- f) Incidence of hepatic encephalopathy after transjugular intrahepatic portosystemic shunt
- g) Impact of stents coating on stenoses incidence in transjugular intrahepatic portosystemic shunt (TIPS)
- h) Study of the quality of life in patients with TIPS
- i) Markers of insulin dependent diabetes mellitus in patients with autoimmune hepatopathy
- j) Impact of hemodynamic changes induced by TIPS on insulin resistance in diabetic patients
- k) Incidence of hemochromatosis among patients with chronic liver diseases

Project was supported by Ministry of Education, No MSM 11150003.

Address for correspondence: Z. Červinková, Dept. of Physiology, Charles Univ. in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Guided tissue regeneration in dentistry - clinical and biological aspects

Grant Agency: Ministry of Health

Project Number: 4802-3/98

Principal Researcher: Ivo Dřížhal

Joint Researchers: Miroslav Červinka, Pavel Měříčka, Radovan Slezák, Petr Bednář, Maher Taha

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2 055 000

Summary of 2000 results

Title of the presentation: Guided tissue regeneration in dentistry - clinical and biological aspects

Authors: Ivo Dřížhal (1), Miroslav Červinka (2), Pavel Měříčka (3), Radovan Slezák (1), Petr Bednář (1), Maher Taha (1)

Fac. Med., Charles Univ., Hradec Králové: (1) Dept. of Dentistry, (2) Dept. of Medical Biology and Genetics, (3) Tissue Bank

The authors in the frame of this research project have performed:

1. the treatment of 48 teeth with periodontal pockets
2. the augmentation of alveolar ridge in 60 patients
3. the testing of the materials used for guided tissue regeneration:
- Gore-Tex (fy Gore), Resolut (fy Gore), Bio-Gide (fy Geistlich), Bass (fy Lasak), Bio-Oss (fy Geistlich), DFDBA (Tissue Bank, Hradec Králové), Vicryl (fy Johnson and Johnson)

Summary of results:

1. Treatment of periodontal pockets:
 - a) the depth of periodontal pockets decreased from 7,0 mm to 2,7 mm
 - b) the attachment level has changed from 9,3 mm to 5,6 mm (gain 3,7 mm)
2. Augmentation of alveolar ridge.
Exposure of membranes:
Vicryl 65 %
Gore-Tex 20 %
Bio-Gide 27 %
3. Testing of material has revealed a toxic properties on tissue cultures.

Project was supported by the Ministry of Health Grant Agency, No 4802-3/98.

Address for correspondence: Ivo Dřížhal, Dept. of Dentistry, Faculty Hospital, Hradec Králové, 500 05, Czech Republic

Title of the research project: Detection of vesicoureteric reflux with contrast ultrasound cystography

Grant Agency: Ministry of Health

Project Number: 4688-3/98

Principal Researcher: doc. MUDr. Pavel Eliáš, CSc.

Joint Researchers: doc. MUDr. Oldřich Pozler, CSc., MUDr. Pavel Rejtar, MUDr. Sylva Skálová, MUDr. Ivo Novák

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 860000

Summary of 2000 results

Title of the presentation: Diagnostic Accuracy of Contrast Enhanced Ultrasound Cystography in the Diagnosis of Vesicoureteral Reflux - Final Results

Authors: Pavel Eliáš (1), Pavel Rejtar (1), Leoš Ungermann (1), Oldřich Pozler (2), Sylva Skálová (2), Ivo Novák (3)

Fac. Med., Charles Univ., Hradec Králové: Dept. Radiology (1), Dept. Pediatrics (2), Dept. Urology (3)

Purpose: To evaluate the diagnostic accuracy of contrast enhanced ultrasound cystography with ascending administration of Levovist (CUSC) for the detection of vesicoureteral reflux (VUR) in children.

Materials and methods: Between September 1998 and August 2000 we performed 71 CUSC examinations in 70 children with either intermitent urinary tract infections or unexplained dilatation of pyeloureteral systems. Based on results of micturating x-ray cystourethrography (MCUG), which served as a "gold standard" in this prospective unbiased study, we evaluated 141 pyeloureteral units.

Results: MCUG revealed 65 refluxing pyeloureteral units. CUSC detected 54 of them, moreover, there were 2 false positive results. Among 11 false negatives, we met only those of grade I (1), grade II (6) and grade III (4) VUR. The parameters of diagnostic accuracy of CUSC for depicting VUR in comparison to MCUG were as follows: sensitivity 83 %, specificity 97 %, positive predictive value 96 %, negative predictive value 97 %, accuracy 92 %.

Conclusion: Contrast enhanced ultrasound cystography is a clinically useful method for depiction of VUR without exposing children to ionising radiation.

Key words: vesicoureteral reflux-children-ultrasonography-ultrasound contrast agents

Address for correspondence: P. Eliáš, Dept. of Radiology, University Hospital, 500 05, Hradec Králové, Czech Republic, E-mail: elias@fnhk.cz

Title of the research project: Contact Photoallergy As a Reason of Some Dermatoses

Grant Agency: Ministry of Health

Project Number: 4689-3

Principal Researcher: MUDr. Karel Ettler, CSc.

Joint Researchers: doc.MUDr. Marie Nožičková, CSc., MUDr. Jaroslava Vaněčková

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 678900

Summary of 2000 results

Title of the presentation: Photo-patch tests as a standard method for detecting the cutaneous photoallergic reactions

Authors: Karel Ettler, Marie Nožičková, Jaroslava Vaněčková, Vlasta Tluková

The epidemiology of contact photoallergy in our population is not well known at present. Therefore the basic aim of our project was to establish the scale of diagnostic methods in the assesment of skin photosensitivity due to contact photosensitive reaction. By means of photo-patch testing we used double-set of 23 substances (Trolab set). These substances were applied to the skin of proband's back to produce contact or/and photocontact response. After 48 hours one test battery has been irradiated by suberythematous dose of UVA (usually 5 J/cm²). We investigated 35 probands who were divided into two groups according to the presence or absence of photosensitivity troubles. Photosensitive group enrolled 24 persons, 11 persons had no symptoms of photosensitivity (controls). Contact sensitization alone was detected in 13 cases in photosensitive group (46%), though 5 controls gave similar incidence of contact responses (45,5%). However reading of phototest results revealed 6 photoallergic responses in photosensitive group. Only 2 photoallergic reactions were present in the group of controls. The sunscreens (propanedione, cinnamates and oxybenzone) were the most frequent photoallergic substances. The other potent contact sensitizer was Fragrance Mix (6 reactions - 17,1%) in our both groups together. We have tested also 779 patients with common contact sensitivity difficulties during 3 years. Positive responses to Fragrance Mix were detected in 108 cases (13,9%). Our data suggest high incidence of contact sensitivity in patients with dermatological problems. Even some photosensitive troubles could be caused by the skin response against photoactivated sunscreen's ingredients. Thus the physical (non-photoallergic) forms of sunscreens should be strongly recommended in essentially photosensitive people especially when underwent local photoprotection since childhood.

Address for correspondence: K. Ettler, Dept. of Dermatology, Charles University, Pospíšilova tř. 365, 500 05 Hradec Králové

Title of the research project: Chronic gastritis induced by Helicobacter pylori infection and/or by autoimmune mechanisms – a source of dyspeptic complaints?

Grant Agency: Ministry of Health

Project Number: NK/6174-2

Principal Researcher: prof. MUDr.Bohumil Fixa,DrSc.

Joint Researchers: MUDr. Olga Komárková, prof. MUDr.Zdeněk Nožička,DrSc., MUDr. Jan Nožička, Irena Šulcová, prof. MUDr. Jaroslav Malý,CSc.

Starting date: 1.1.2000

Duration (years): 2

Funds allocated for project - total in Czech crowns: 650000

Summary of 2000 results

Title of the presentation: Gastric autoimmunity , its specification under the new aspects of gastric autoantibodies examination.

Authors: Bohumil Fixa (1), Olga Komárková (1), Zdeněk Nožička (2), Jan Nožička (2)

Fac.Med.Charles Univ., Hradec Králové: 2nd Department of Medicine (1), Institut of Pathology (2)

The objective of the work was to evaluate the relationship of newly described gastric autoantibodies (anticanalicular and antiluminal) to antibodies against the cytoplasm of parietal cells assessed in the traditional way (antimicrosomal antibodies), and to evaluate at the same time their relationship to the gastric mucosa and infection with Helicobacter (H.) pylori. This study should be a base for the study of autoimmune gastritis and dyspepsia. A total of 56 patients selected from about 1000 patients examined originally for gastric autoantibodies were included into the study.

The presence of anticanalicular gastric antibodies seems to be more accurate for the evaluation of gastric autoimmunity than the presence of antimicrosomal antibodies, but no gastric autoantibody provides precise information of the state of the gastric mucosa. Rarely, normal gastric mucosa can be accompanied with gastric autoantibodies and conversely, the autoimmune type of chronic gastritis may exist without gastric autoantibodies. H.pylori was evident in 58.3% of the patients with gastric autoantibodies.

When we try to evaluate the participation of autoimmune gastritis on dyspepsia, the present experience should be considered.

Literature:

Fixa, B., Komárková, O., Nožička, Z., Petrová, J., Faller, G.: Relationship of gastric autoantibodies, the state of the gastric mucosa and Helicobacter pylori infection. Gut 2000, 47 (Suppl.III): A107

Address for correspondence: prof. MUDr. B. Fixa, DrSc., 2nd Dept. of Internal Medicine, Pospíšilova str. 360, 500 05 Hradec Králové

Title of the research project: Long term influence of hemodialysis and peritoneal dialysis on immunity of patients with chronic renal failure.

Grant Agency: Ministry of Health

Project Number: NK4565-3

Principal Researcher: MUDr. Petr Fixa, CSc.

Joint Researchers: MUDr. Božena Hájková, CSc., MUDr. Vladimír Herout, MUDr. Otakar Kopecký, CSc., doc. RNDr. Jan Krejsek, CSc.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 742000

Summary of 1998 results

Title of the presentation: Long term influence of hemodialysis and peritoneal dialysis on immunity of patients with chronic renal failure.

Authors: Petr Fixa (1), Božena Hájková (1), Vladimír Herout (1), Otakar Kopecký (2), Jan Krejsek (2)

1st Clinic of Medicine, Faculty Hospital, Hradec Králové (1), Dept. of Clinical Immunology and Allergology (2), Faculty Hospital, Hradec Králové

Study had two objectives:

The first objective was to contribute to the knowledge of and to describe immune reactions of patients with chronic renal failure treated by regular hemodialysis (HD), continuous ambulatory peritoneal dialysis (CAPD) and patients before starting renal replacement therapy (CRF). The second objective was to establish especially the influence of regularly used dialysis membranes on immune responses patients on HD.

Methodology:

Study was opened for all patients with CRF starting HD or CAPD. HD patients were divided to 2 groups (A and B) not differing in age, gender, diagnosis and basic parameters of HD, especially Kt/V. A. group was treated only by cuprophane (CU) membranes, B. group only by polysulphone (PSF) membranes. All patients were investigated by the set of immunological tests before starting, in 4 and 12 weeks, 6 and 12 months of the treatment.

(CD3+, CD4+, CD8+, CD3+DR+, CD4+CD45Ro+, TCRA/B,G/D, CD5+19+, CD23+19+, CD11a,b,c, CD14+/38+, NK cells, phagocytosis, bactericidia, spont. and PHA stim.T cell activation, IL-1, 2, 4, 6, 8, MCP-1, MIP-1, TNF, neopterin, VCAM1, ICAM1).

Results:

During HD treatment increased counts of all subpopulations of T cells compared with CRF, no changes were found in T cell activity (except of increase in the first month). No significant changes were found in phagocytosis, and bactericidia.

No significant differences were found between CU and PSF in all these parameters.

Project was supported by Grant Agency of Ministry of Health, No NK4565-3.

Address for correspondence: MUDr. Petr Fixa, CSc., I. interní klinika FN, 50005 Hradec Králové, Czech Republic

Title of the research project: New Iron Chelators - Problems of Their Cardiovascular, Potential Cardioprotective and Biotransformation Effects.

Grant Agency: Czech Republic

Project Number: 305/00/0365

Principal Researcher: Vladimír Geršl

Joint Researchers: Přemysl Poňka, Eva Kvasničková, Radomír Hrdina, Yvona Mazurová, Michaela Adamcová, Jana Kaplanová, Jarmila Macháčková

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 4495000

Summary of 2000 results

Title of the presentation: Effects of 10-week pyridoxal isonicotinoyl hydrazone administration on selected organ systems in rabbits.

Authors: T. Šimůnek (1), I. Klimtová (1), V. Geršl (3), R. Hrdina (1), L. Schrötterová (2), E. Kvasničková (2), Y. Mazurová (4), M. Adamcová (5), J. Macháčková (3), J. Kaplanová (6)

Charles Univ.: Fac. Pharm., Hr. Králové: Dept. of Pharmacol (1), Dept. of Biochem. (2); Fac. Med., Hr. Králové: Dept. of Pharmacol. (3), Dept. of Histol. Embryol. (4), Dept. of Physiol. (5), Dept. of Pediatrics (6)

The aim of the study was to determine effects of repeated administration of pyridoxal isonicotinoyl hydrazone (PIH), an iron chelator, on cardiovascular, haematological and biochemical parameters, and activities of some biotransformation isoenzymes P450 in vivo. PIH (50mg/kg) was administered to the Chinchilla male rabbits i.p., partially dissolved in 10% Cremophor solution in water, once weekly, 10 weeks. The control group received i.p. 10% Cremophor solution in water (2ml/kg). There were no differences observed in the values of the pre-ejection period, left-ventricular ejection time, and the PEP/LVET ratio, in the both groups during the whole study. At the end of the study, arterial blood pressure in the PIH group was significantly higher (by 19.6%) compared with the control group. PIH induced only occasional transient significant changes, without any consistent trends, in most of the followed biochemical and haematological parameters. The activities of all the P450 isoenzymes studied were significantly decreased (1A1 isoenzyme to 29.6% of the control value, 1A2 to 25.4% and 3A to 15.6%) except the 2B isoenzyme (51.1%). The body weight in the PIH group remained nearly identical during the experiment in comparison with the significant increase in the body weight in the controls (by 13%). The histological evaluations of heart, kidney, liver, lung and doudenum revealed no pathological changes. It is possible to conclude that PIH seems to be relatively non-toxic, however, further investigations are necessary to confirm this suggestion.

Project was supported by the Grant GA CR No 305/00/0365 and by the Research Project MSM J13/98:111500001.

Address for correspondence: V. Geršl, Dept. of Pharmacology, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Rep.

Title of the research project: Pharmacokinetic of low dose methotrexate administered to patients in early stage of disease

Grant Agency: Charles University

Project Number: 31056

Principal Researcher: MUDr. Jiří Grim

Joint Researchers: Prof. MUDr. Jiřina Martínková, CSc., MUDr. Marie Šimková, MUDr. Jaroslava Vaněčková, MUDr. Věra Koudelková, Doc. MUDr. Marie Nožičková, CSc.

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 170000

Summary of 2000 results

Title of the presentation: Pharmacokinetic of low dose methotrexate, administered to patients in early stage of disease

Authors: MUDr. Jiří Grim (1), Prof. MUDr. Jiřina Martínková, CSc. (1), MUDr. Marie Šimková (2), MUDr. Jaroslava Vaněčková (2), MUDr. Koudelková (2)

1 - Department of Pharmacology, Charles University, Faculty of Medicine

2 - Department of Dermatovenereology, Charles University, Faculty of Medicine

LDMTX is generally accepted as a second-line agent for the treatment of psoriasis that is unresponsive to tar and retinoids. The aim of this prospective, randomized parallel-group study was to investigate the PK and PD of oral LDMTX in patients suffering from severe and resistant form of psoriasis. The study was approved by a local Ethic Committee and an informed consent was obtained. The patients were assigned to 2 regimens of either 7.5 mg or 15 mg MTX a week given in 3 equal doses separated by 12h. PK were evaluated after doses no. 1 and 39 (i.e. 1st and 13th weeks of treatment, periods 1 and 2). Blood was sampled at 0, 1, 2, 4, 8 and 12h and urine was collected over the interval 0-12h postdose. MTX in plasma and urine was determined using HPLC (Chládek et al., 1997). PD were assessed at baseline and after 13 weeks of therapy using psoriasis area and severity index (PASI). Two-way ANOVA (factors: subject and period) on the log-transformed AUC0-12h showed no effect of period ($p=0.86$). Moreover, the intra-individual variability in AUC0-12 was 6-fold less than the inter-individual variability ($p<0.0005$). Therefore, further analyses were performed using the PK variables observed in the phase 1. Renal clearance (CLR) accounted for $77\pm 23\%$ of the MTX total clearance (CLT). There was a linear relationship ($r_2 = 0.50$, $p<0.001$) between CLR and creatinine clearance (CLCR). PK/PD analysis revealed a significant inverse relationship between PASI and AUC0-12h ($\rho = -0.68$, $p<0.001$). Fifteen subjects (5 from the group 7.5 and all 10 from the group 15) achieved higher than 50% drop in PASI and were classified as responders. Thirteen out of 15 responders had AUC0-12 higher than 600 nmol.h/l as compared with none of 4 nonresponders.

Address for correspondence: MUDr. Jiří Grim, Department of Pharmacology, Charles University, Faculty of Medicine in Hradec Králové

Title of the research project: Some hormonal and metabolic changes during the conversion period of parenteral and enteral nutrition

Grant Agency: Ministry of Health

Project Number: 4788-3/98

Principal Researcher: MUDr. Eduard Havel

Joint Researchers: Doc. MUDr. Luboš Sobotka, CSc., MUDr. Jan Maňák, Doc. MUDr. Vladimír Bláha, CSc., MUDr. Radomír Hyšpler, PhD., RNDr. Dagmar Solichová, Prof. MUDr. Zdeněk Zadák, CSc.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2036000

Summary of 2000 results

Title of the presentation: Some metabolic and hormonal aspects of enteral nutrition

Authors: Eduard Havel (1), Luboš Sobotka (1), Vladimír Bláha (1), Dagmar Solichová (1), Radomír Hyšpler (1), Zdeněk Zadák (1)

Fac. Med., Charles Univ., Hradec Králové, Dept. of Gerontology and Metabolic care (1)

Enteral nutrition is popular in intensive care. Keeping the intestine in function by feeding stimulation helps to treat intensive care patients. We aimed to find metabolic and hormonal differences between enteral and parenteral feeding.

Design: 20 cardiopulmonary stable patients hospitalised at the Metabolic Department of Teaching Hospital in Hradec Králové were monitored in a prospective study.

Interventions: The patients, who were fed more than two weeks parenterally without enteral feeding due to their disease (mostly uncomplicated intestinal fistula after surgical intervention with possibility to start enteral feeding), were studied after obtaining informed consent. The parenteral nutrition was fortified by 4200 kJ parenterally in days 0. - 2. and next enterally in the same contents (Nutrison 1000 ml) in days 7. -14. The local Ethics committee approved this research project.

Measurement and methods: Comparisons between parenteral+parenteral period and parenteral+enteral period in several serologic and urine parameters were calculated.

Wilcoxon's pair t-test was used for statistical analysis.

Results: HDL cholesterol (0,61 vs 0,72 mmol/l), apoprotein A (0,63 vs 0,71 g/l) and insulin like growth factor – IGF-1 (291,7 vs 321,4 ng/ml) were significantly higher in enteral period ($p < 0,05$). The urinary output of urea (551 vs 489 mmol/day), P (31 vs 24 mmol/day), Na (418 vs 220 mmol/day) were significantly lower during enteral period ($p < 0,05$).

Conclusion: Enteral nutrition application is associated also with some anabolic effects in comparison to application of parenteral nutrition alone. The higher level of IGF-1 is main anabolic marker of enteral nutrition in our study. The decline of urea output means an enhanced proteosynthesis (probably most in intestine mass). Higher level of HDL during enteral feeding we explain by the enhanced synthesis of cholesterol.

Address for correspondence: MUDr. Eduard Havel, Dept. Gerontology and Metabolic Care, Fac. Med., Charles Univ., Sokolská 581, 500 05 Hradec Králové, Czech Republic

Title of the research project: Intraoperative Radioimmunodetection of Colorectal Cancer

Grant Agency: Ministry of Health

Project Number: 4532-3

Principal Researcher: MUDr. Pavel Hladík

Joint Researchers: MUDr. Ing. Jaroslav Vižďa , Doc. MUDr. Luboš Sobotka, CSc.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 892000

Summary of 2000 results

Title of the presentation: Intraoperative Radioimmunodetection of Colorectal Cancer

Authors: Pavel Hladík (1), Jaroslav Vižďa (2), Luboš Sobotka (3).

Dept. of Surgery (1), Dept. of Nuclear Medicine (2), Dept of Metabolic Care and Gerontology (3), Teaching Hospital, Charles University, Hradec Králové

INTRODUCTION: Immunoscintigraphy is one of the preoperative diagnostic methods used in the treatment of colorectal cancer. The intraoperative detection of radiolabelled monoclonal antibodies radioactivity by hand-held probe can discover other sites with occult lymph-node metastases. The aim of the study is to evaluate the pre and intraoperative diagnostic results according to postoperative histology examination.

METHODS: 121 colorectal cancer patients were operated on using RIGS (radioimmunoguided surgery). Two radiopharmaceuticals were used. Oncoscint 103 (111-In) and CEA-Scan (99m-Tc). The immunoscintigraphy as the whole body scan and SPECT of abdomen was performed after radionuclide i.v. administration. Intraoperative radioactivity was detected by hand-held gamma-probe. In histological investigation were used classical H&E staining and immunohistochemical method.

RESULTS: The relations between the RIGS positive results and histological examinations were statistically assessed after the 38th operation. Analyses used the programme NCSS. All subsequent results were evaluated by the most acceptable and statistically confirmed method. Immunoscintigraphy was negative in 5 cases (4.1%). 55 RIGS positive results were confirmed by 43 histologically positive examinations (78%). In this group 9 cases were confirmed by immunohistochemistry. In the group of 66 RIGS negative results were 4 histologically positive results (6.1%).

CONCLUSIONS: While treating the primary tumorous disease the use of RIGS may help in assessment of necessary extent of operation performance and in staging of the disease by revealing even the occult lymph nodes involved. In the case of recurrent malignant disease especially immunoscintigraphy enable to make diagnostics more accurate.

Project is supported by the Czech Republic Ministry of Health (MZ IGA 4532-3)

Address for correspondence: P. Hladík, Dept. of Surgery, Teaching Hospital, Charles University, Hradec Králové, 500 05, Czech Rep., E-mail: hladikp@lfhk.cuni.cz

Title of the research project: Metabolism of proteins and branched-chain amino acids in renal insufficiency - therapeutic possibilities.

Grant Agency: Czech Republic

Project Number: 306/98/004

Principal Researcher: Doc. MUDr. Milan Holeček, CSc.

Joint Researchers: Doc. MUDr. Vladimír Teplan, CSc., Ing. Luděk Šprongl, RNDr. Ing. František Skopec, CSc., Doc. MUDr. Ivan Tilšer, CSc., Doc. RNDr. Miloš Tichý, CSc., MUDr. Veronika Listíková, CSc., MUDr. Vendula Mikesková, MUDr. Roman Šafránek

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2387000

Summary of 2000 results

Title of the presentation: Protein and BCAA metabolism in renal insufficiency.

Authors: Milan Holeček (1), Luděk Šprongl (2), Ivan Tilšer (3), Roman Šafránek (1) and Miloš Tichý (4)

Departments of (1) Physiology and (4) Medicine, Charles University Prague, Medical Faculty, Hradec Králové, (3) Pharmaceutical Faculty, Hradec Králové, and (2) University Hospital Motol, Prague, Czech Republic

Changes in protein and amino acid metabolism were estimated using L-[1-14C]leucine in rats with acidosis induced by infusion of 0.2 M HCl, in acute renal failure induced by bilateral nephrectomy (BNX), and in chronic renal failure induced by 5/6 nephrectomy.

In rats with acidosis induced by HCl infusion a marked increase in protein turnover (increase in proteolysis and protein synthesis) and leucine oxidation were observed.

BNX caused significant decrease in protein synthesis in skeletal muscle, decrease in whole-body protein breakdown, decrease in protein synthesis, and a decrease in leucine clearance. In addition, a marked increase in leucine oxidized fraction caused by the decreased rate of leucine incorporation in body proteins was observed in BNX rats.

Acidosis and characteristic markers of chronic renal failure appeared in blood plasma in 30 % of rats with 5/6 nephrectomy within 28 weeks while in 70 % of animals with 5/6 nephrectomy insignificant changes in acid-base balance were detected. Significant decrease in plasma levels of branched-chain amino acids (BCAA) was observed in all rats with 5/6 nephrectomy. However, only in rats with acidosis significant increase in whole-body proteolysis, leucine clearance and leucine oxidation was demonstrated.

It is concluded that (1) acidosis and activated BCAA oxidation are an important factor in protein wasting development and (2) changes in protein and amino acid metabolism in BNX rats are remarkably different to those observed in rats with 5/6 nephrectomy.

References:

Holeček et al. Res. Exp. Med. (in press)

Holeček et al. Exp. Toxicol. Pathol. (submitted)

Supported by the grant No. 306/98/0046 of the Grant Agency of the Czech Republic.

Address for correspondence: Dr. Milan Holeček, Department of Physiology, Charles University, School of Medicine, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Protein metabolism in hepatic injury and possibilities of influencing of liver regeneration by intervention in metabolism of amino acids.

Grant Agency: Charles University

Project Number: 276/98C

Principal Researcher: Doc.MUDr. Milan Holeček, CSc.

Joint Researchers: Ing. Luděk Šprongl
RNDr. Ing. František Skopec, Csc.
Doc.MUDr. Ivan Tilšer, CSc.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 770000

Summary of 2000 results

Title of the presentation: Protein and amino acid metabolism in hepatic injury and possibilities of influencing liver regeneration by intervention in metabolism of amino acids

Authors: Milan Holeček (1) and Luděk Šprongl (2)

Departments of (1) Physiology Charles University Prague, Medical Faculty, Hradec Králové and (2) University Hospital Motol, Prague, Czech Republic

The aim of the project is to obtain new information concerning the pathogenesis and therapeutical significance of disturbances in amino acid metabolism in liver injury. Using male Wistar rats we evaluated (1) the effect of severity of liver injury, (2) the effect of hyperammonemia, and (3) the effect of impairment in methionine metabolism.

(1) Liver injury was induced by CCl₄ (2, 4 or 6 g/kg). In the phase of the development of liver damage (16 and 24 h), an increase in blood amino acid levels and positive correlations with the dose of CCl₄ were observed for most amino acids. At a phase of liver recovery (48 and 96 h), the concentrations of some amino acids decreased below the control values.

(2) Hyperammonemia induced by ammonium infusion caused an increase in glutamine and a decrease in BCAA and alanine in plasma, a more significant decrease in whole-body protein synthesis than in whole-body proteolysis, and an increase in leucine oxidized fraction. We conclude that the decrease in plasma BCAA after ammonia infusion is associated with decreased proteolysis and increased leucine oxidized fraction. The more significant decrease in protein synthesis than in proteolysis imply protein wasting in the hyperammonemic rats.

(3) The impairment in liver regeneration was observed in buthionine sulfoximine (BSO, inhibitor of glutathione synthesis) treated rats. S-adenosylmethionine induced an earlier onset of hepatocyte mitotic activity and reduced the inhibitory effect of BSO. Glutathione exerted an inhibitory effect on liver regeneration and worsened the negative effect of BSO.

References:

1. Holeček M. et al. Amino Acids 161: 1-11, 1999
2. Holeček M. et al. Metabolism 49: 1330-4, 2000
3. Holeček M. et al. Arzheim.-Forsch. Drug Res. (in press)

Address for correspondence: Dr. Milan Holeček, Department of Physiology, Charles University, School of Medicine, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Immunoblot Configuration as a Confirmative Serological Method in the Diagnosis of Lyme Borreliosis.

Grant Agency: Ministry of Health

Project Number: 4549-3

Principal Researcher: MUDr. Honegr Karel

Joint Researchers: RNDr. Dagmar Hulínská, Doc. MUDr. Václav Dostál, Doc. RNDr. Jan Krejsek, CSc, RNDr. Marcela Drahošová, Mgr. Jana Havlasová, MUDr. Pavel Gebouský

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 940000

Summary of 2000 results

Title of the presentation: Immunoblot Configuration as a Confirmative Serological Method in the Diagnosis of Lyme Borreliosis.

Authors: Karel Honegr (1), Jana Havlasová (2) Pavel Gebouský (1), Václav Dostál (1), Věra Pellantová (1) Zuzana Škrabková, (3) University Hospital, Hradec Králové: Department of Infectious Diseases (1), Dept. of Clinical Immunology (2), FM-Computer Technology Center(3).

The clinical manifestations of Lyme borreliosis are mostly not pathognomic. Therefore the reliable laboratory tests are necessary for the clinical diagnosis support. A two-step approach for the serological diagnosis of Lyme borreliosis has recently been proposed. All specimens with positive or equivocal results should be confirmed using the immunoblot. The analysis of Western blot results is complicated by the lack of the established criteria for the interpretation of European Lyme borreliosis blots. The aim of the study: To demonstrate the diagnostic importance of the antibodies production against specific antigens of three *Borrelia burgdorferi* genotypes manifested in various clinical forms of Lyme borreliosis in the Czech republic. After the analysis of result we determined, whether the only one genotype with a high level of reliability can be used or whether is necessary to use all of them. The serum samples of 63 patients suffering from Lyme borreliosis have been collected. The serum samples will be examined by immunoblot made from the three genotypes of *Borrelia burgdorferi* sensu lato. The check group consists of 40 healthy blood donors, which serums have already been examined. Backward stepwise logistic regression analysis was used to determine the best independently discriminated bands among the *Borrelia burgdorferi* serum and those without. The rules have been made according to the subset of the independently significant bands, their sensitivities and specificities have been assessed. To establish criteria for the positive WB result, the discriminating ability of the band series combination (interpretation rules) have been evaluated separately for the each strain.

Robertson, J.; Guy, E.; Andrews, N.: A European multi-centre comparison of immunoblot in the serodiagnosis of Lyme borreliosis. J. Clin. Microbiol., 2000, Jun;38(6):2097-102.

Address for correspondence: Honegr@LFHK.cuni.cz

Title of the research project: Preclinical teaching innovation in modernized phantom lab

Grant Agency: Ministry of Education

Project Number: 1849/2000

Principal Researcher: Věra Hubková

Joint Researchers: Radovan Slezák

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 1362000

Summary of 2000 results

Title of the presentation: Preclinical teaching innovation in modernized phantom lab

Authors: Věra Hubková, Radovan Slezák

Fac. Med., Charles Univ., Hr. Králové: Dept. of Dentistry

The simulation system helps the students to obtain necessary manual training during the preclinical practice. The system perfectly imitates the dental chair particularly with its technical equipment. The phantom head with the oral opening and dental arches simulates the patient.

The student of dentistry has the opportunity to train the preparations in restorative and prosthetic dentistry (in both jaws), endodontic treatment, extraction of the teeth and calculus removal, impression technique of dentate, partially dentate and edentulous jaw and jaw relationship recording. It is appropriate for the students to provide all kinds of treatment in pairs. One of them is working as a dentist, the other one as an assistant. This is the way how the four handed treatment procedure which is both economic and ergonomic method in dental practice can be trained.

The preclinical simulation system education manifests mainly as the effective practical training before the clinical practice, because of uncomparably better preparation of the student for the real patient treatment.

Project was supported by the Ministry of Education Grant Agency, No 1849/2000.

Address for correspondence: V. Hubková, Dept. of Dentistry, Faculty Hospital, Hradec Králové, 500 05, Czech Republic

Title of the research project: Haemodynamic, clinical and biochemical assessment of patients before and after Transjugular Intrahepatic Portosystemic Shunt (TIPS) - part II

Grant Agency: Ministry of Health

Project Number: NA/4558-3

Principal Researcher: doc. MUDr. Petr Hůlek, CSc.

Joint Researchers: doc. MUDr. Antonín Krajina CSc., MUDr. Václav Šafka, PhD., MUDr. Jozefína Dufincová, Prof. MUDr. Jiří Kvasnička, CSc.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 611000

Summary of 2000 results

Title of the presentation: Haemodynamic, clinical and biochemical assessment of patients before and after TIPS

Authors: Petr Hůlek (1), Antonín Krajina (2), Václav Šafka (3), Tomáš Fejfar (1), Jozefína Dufincová (1), Jiří Kvasnička (1)

(1) 1st Department of Internal Medicine, (2) Department of Radiology, (3) Department of Physiology

TIPS as a small-diameter non-surgical shunt takes an important place in the treatment of clinically significant portal hypertension. The aim of the project was: 1. to compare covered and non-covered stents in development of in-stent stenosis, 2. to determine the incidence and risk factors for development of hepatic encephalopathy (HE), 3. to determine influence of TIPS on insulin resistance (IR), 4. to confirm the haemodynamic changes after TIPS. Material and methods: There were 336 patients treated by TIPS from 1992 to September 2000. TIPS was performed in 81% of patients for bleeding into the gastrointestinal tract caused by portal hypertension (24% urgently), 18% of patients for refractory ascites. Results: 1. We used 45 (14%) covered stents with statistically lower occurrence of in-stent stenosis ($p=0,01$). 2. Incidence of HE was 33,2%. There were 9% of the patients who underwent a procedure of reducing the diameter of TIPS because of HE. The age ($p=0,002$) and the non-alcoholic etiology of the liver cirrhosis ($p=0,05$) meant statistically significant higher risk for development of HE in our group of patients. HE was not influenced by other follow-up parameters. 3. We measured the changes in IR after TIPS by hyperinsulin euglycemic clamp in 22 patients. The first results showed that there are no significant changes in insulin resistance after TIPS and no significant differences between diabetics and non-diabetic patients. 4. By measurement of haemodynamic parameters we found statistically significant increase in cardiac output ($p=0,007$) and cardiac index ($p=0,001$) one day after TIPS. Conclusion: Continuing in the long-term follow-up of patients after TIPS is very important. TIPS as a perspective method for treatment of complications of portal hypertension needs to establish more precise criteria, especially in urgent indication.

Address for correspondence: Petr Hůlek, MD, 1st Department of Internal Medicine
University hospital, 500 05 Hradec Králové

Title of the research project: Assessment of dipeptidylpeptidase IV in thyroid tumors - its importance in differential diagnosis

Grant Agency: Charles University

Project Number: 87/2000/C

Principal Researcher: Ivana Kholová

Joint Researchers: Ivo Šteiner, Aleš Ryška, Jan Čáp, Marie Ludvíková, Lucie Barvířová

Starting date: 1.4.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 100000

Summary of 2000 results

Title of the presentation: Dipeptidylpeptidase IV in thyroid differential diagnosis

Authors: Ivana Kholová (1), Aleš Ryška (1), Jan Čáp (2), Marie Ludvíková (3)

Fac. Med., Charles Univ., Hr. Králové: Fingerland Dept. of Pathology (1), Dept. of Internal Medicine (2), Fac. Med., Charles Univ., Plzeň: Šíkl's Dept. of Pathology (3)

The aim of the project is to evaluate possible role of dipeptidyl aminopeptidase IV (DPP IV) in distinguishing between benign and malignant thyroid tumors.

DPP IV is a highly specific membrane protease not present in normal follicular cells.

However, aberrant expression of DPP IV was reported in malignant thyroid lesions.

We have stained for DPP IV (Lojda and Aratake method) 100 cytologic specimens (aspiration and imprint smears) and 91 cryostat sections. The staining pattern of a minimum of 200 follicular cells per smear was evaluated. The results were correlated with subsequent histological diagnosis and statistically analysed. In cytology, threshold 0%, 5%, and 50% of positive follicular elements was tested. The sensitivity was 98.2%, 82.1%, and 70.0%, the specificity was 55.8%, 88.9%, and 98.8%, the positive predictive value was 60.9%, 71.9%, and 93.3%, and negative predictive value was 97.7%, 93.5%, and 93.1%, respectively. In cryostat sections, the results were classified only as positive or negative (threshold 0%). The sensitivity was 83.3%, the specificity was 82.5%, the positive predictive value was 64.1%, and the negative predictive value was 93.0%, respectively.

This technique may have great potential in distinguishing between benign and malignant thyroid tumors, both in preoperative and intraoperative smears and cryostat sections.

Project was supported by the Charles University Grant Agency, No 87/2000/C

Address for correspondence: I. Kholová, Fingerland Dept. of Pathology, Charles University Medical Faculty Hospital, CZ-500 05 Hradec Králové, Czech Republic, kholova@fnhk.cz

Title of the research project: Intestinal permeability in patients with inflammatory bowel diseases - the role in pathogenesis and monitoring of the course of the disease and its treatment

Grant Agency: Ministry of health Czech Rep. **Project Number:** 4529-3

Principal Researcher: MUDr Pavel Kohout, Ph.D.

Joint Researchers: MUDr Helena Brodská, doc MUDr Jan Bureš, CSc, MUDr Radomír Hyšpler, MUDr Pavel Koref, MUDr Rudolf Repák, MUDr David Tuček, prof MUDr Zdeněk Zadák, CSc

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 418000

Summary of 2000 results

Title of the presentation: Small bowel permeability in patients with inflammatory bowel diseases

Authors: Pavel Kohout (1), Radomír Hyšpler (1), Pavel Koref (1), David Tuček (1), Zdeněk Zadák (1), Jan Bureš (2), Rudolf Repák (2), Helena Brodská (3), Aleš Novotný (4)

University Hospital of Charles University Hradec Králové, Dept. of Gerontology and Metabolic Care (1), IInd Department of Internal Diseases (2), University Hospital of Charles University Praha, Dept. of Biochemistry (3), IVth Department of Internal Diseases

The ground of small bowel permeability test is the measurement of absorption of sugars with different size of molecules through the bowel wall. The increased permeability was found in patients with diseases with damaged intestinal barrier (untreated celiac sprue, Crohns disease and ulcerative colitis both at the acute inflammatory phases).

Index of small bowel permeability was counted as lactulose/mannitol ratio of sugars absorbed from the gut and excreted into urine during 5 hours.

135 patients with Crohns disease and ulcerative colitis were examined during 3 years, there were performed 435 measurements. We found the correlation between the value of small bowel permeability and markers of inflammation and the inverse correlation between permeability and markers of nutrition.

In patients with untreated celiac sprue there is small bowel permeability increased, during the gluten free diet this value decreases. We did not find any differences between the relatives of the patients with IBD and health controll.

Test of small bowel permeability is good noninvasive method for the control of small bowel barrier

Project was supported by Ministry of Health Czech republic, Internal Grant Agency Nr 4529-3

Address for correspondence: Pavel Kohout, MD, PhD,
Department of metabolic care University hospital, Sokolská 408, 500 05 Hradec Králové

Title of the research project: Incorporation of Dental Implantology in the Stomatology Teaching of Faculty of Medicine

Grant Agency: Ministry of Education

Project Number: 1858/2000

Principal Researcher: Dana Kopecká

Joint Researchers: Antonín Šimůnek

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 80000

Summary of 2000 results

Title of the presentation: Incorporation of Dental Implantology in the Stomatology Teaching of Faculty of Medicine

Authors: Dana Kopecká, Antonín Šimůnek

Fac. Med., Charles Univ., Hr. Králové: Dept. of Dentistry

The aim of our study is to perform an implantology program and incorporate it in our pregradual education.

The theoretic part will be introduced in the dental surgery syllabus of the fifth year stomatology program in the summer term. It will have a range of four hours and then it will be included in the preprosthetic surgery program in the fourth year of study.

For the theoretic background we will use audio-visual methods, like slides and folios. Practical part will accomplish in the Implantology Center of the Stomatology Department. The students will attend to the surgical stages and then they will assist during the procedures too. For the practical teaching will be valuable to use a simple models of the implantologic situations including the consequential prosthetic solutions. The prosthodontic treatment related with implants is not like the conventional treatment, and for the students can be very hard to learn their morphology and function. For a good understanding of the procedures to make the prosthodontic structures are necessary amplified models for the clinic and laboratory elements.

In a suitable reduced range, this background will be also for the fourth year students of general medicine.

After the course the stomatology student must be able to have concrete ideas about indications and contraindications in dental implantology, solid knowledge about surgery stages and the prosthetic branch. The medical student would be able to know the possibilities that actually offers dental implantology.

Project was supported by the Ministry of Education Grant Agency, No 1858/2000.

Address for correspondence: D. Kopecká, Dept. of Dentistry, Faculty Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Use of carbon dioxide as a contrast agent for angiography

Grant Agency: Ministry of Health

Project Number: IGAMZ 4545-3

Principal Researcher: Antonin Krajina, M.D.

Joint Researchers:

Miroslav Lojik, M.D.

Jan Raupach, M.D.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: -600000

Summary of 2000 results

Title of the presentation: WEDGED HEPATIC VENOGRAPHY FOR TARGETING THE PORTAL VEIN DURING TIPS: COMPARISON OF CO₂ AND IODINATED CONTRAST AGENTS.

Authors: A. Krajina, M. Lojik, J. Raupach, P. Hulek

Purpose: CO₂ can better traverse the hepatic sinusoids than iodinated contrast medium and has been used by many interventionalists for wedged hepatic venography during TIPS. Our study was designed to compare the extend of the portal vein opacification using CO₂ in one group of patients and iodinated contrast medium in the other group.

Materials and Methods: The wedged hepatic venography for the portal vein opacification during TIPS was performed using hand injection through 6,5F diagnostic catheter.

Portograms of 36 patients performed with 10 ml of iodinated contrast medium were retrospectively compared with portograms of 45 patients performed with 30-40 ml of CO₂.

The opacification of the right portal vein branch including the portal vein bifurcation was assessed as a successful study.

Results: Using CO₂ the right portal vein branch and the portal vein bifurcation was opacified in 87 % patients (in 39 out of 45), only a part of the right portal vein branch was opacified in 4,4 % patients and no opacification of any portal vein branch was in 6,67 % patients. Using iodinated contrast agent there was opacification of the portal vein bifurcation in 25 % patients (in 9 out of 36) and part of the portal vein branch in 36 % and no opacification of any branch was in 39 %. There was one case of hepatic laceration from wedged venography which was treated with microcoil embolization.

Conclusions: Using CO₂ as a contrast medium opacification of the portal vein bifurcation by the wedged hepatic venography was in 87 % in comparison to only 25 % when iodinated contrast medium was used (p

investigators over the iodinated contrast medium for wedged hepatic venography during TIPS.

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Address for correspondence: Department of Radiology, Charles University, Hradec Kralove, 500 05, Czech Republic

Title of the research project:

Multiple drug resistance of leukemia cells and its assessment in vitro

Grant Agency: Ministry of Health

Project Number: M/20-3/98

Principal Researcher: Jan Krejsek

Charles University, School of Medicine, Institute of Clinical Immunology and Allergy

Joint Researchers:

Otakar Kopecký, Karolína Jankovičová, Petr Souček

Charles University, School of Medicine, Institute of Clinical Immunology and Allergy

Jaroslav Malý, Jaroslava Voglová

Department of Haematology, University Hospital

Hradec Králové, Czech Republic

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 505000

Summary of 2000 results**Title of the presentation:**

Multiple drug resistance of leukemia cells and its assessment in vitro

Authors: Otakar Kopecký, Karolína Jankovičová, Petr Souček, Jaroslav Malý,
Jaroslava Voglová

The expression of p-170 marker which is thought to be the principal molecule responsible for multiple drug resistance of malignant cells together with expression of other drug resistance molecules such as MRP and LRP was determined by immunofluorescence technique using flow cytometric analysis. Totally, 37 samples of either bone marrow or peripheral blood of consecutive patients suffered from various types of blood malignancies were examined. The positivity for p-170 molecule expression was found on cells of 19 %, LRP positivity on cells of 51 % cases examined, respectively. The presence of MRP molecule has not been found on cells of any case examined so far.

The test to evaluate function of multiple drug resistance proteins was performed on 13 samples using rhodamine 123 efflux assay. The positivity expressed as MFI index > 1,1 was found in 38 % of samples examined.

The link between multiple drug resistance and apoptosis of leukemia cells is sought using newly established testing procedure. Briefly, malignant cells are cultivated in vitro in the presence of either doxorubicin in the case of acute myelogenous leukemia or chlorambucil in the case of chronic lymphocytic leukemia. Early and late events of apoptosis are measured by flow cytometry. The tests evaluating early steps of apoptosis include determination of caspase 8 and Apo 2.7. and annexin V expression. The late steps of apoptosis are determined by caspase 3 together with TUNEL and propidium iodide tests. Such extensive experiments were performed on cells of 6 patients with AML and 12 patients suffered from CLL.

Finally, collection of selected clinical parameters is now in progress. The ultimate goal of this project will be the correlation of the results of laboratory tests with clinical parameters.

Address for correspondence: Jan Krejsek, Charles Univ., Sch. of Medicine, Institute of Clinical Immunology, Hradec Králové, 500 05, Czech Republic, e-mail:ukia@fnhk.cz

Title of the research project: A system of educational programs for teaching statistics in medical schools

Grant Agency: Ministry of Education

Project Number: 1852/F3/00

Principal Researcher: Iva Krulichová

Joint Researchers: Josef Bukač, Jiří Záhora

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 60000

Summary of 2000 results

Title of the presentation: A system of educational programs for teaching statistics in medical schools

Authors: Iva Krulichová, Josef Bukač, Jiří Záhora

Fac. Med., Charles Univ., Hr. Králové: Dept. of Biophysics

At present, the trend in creating the materials to help students in diverse fields of interest aims towards the use of electronic equipment. One of the many advantages of this approach is the availability of the material to a very wide audience through both the local network and the Internet. The use of computers enables us to include interactive interface, which not just makes the text more readable but also substantially increases student's depth of understanding.

The purpose of the project is to create a program for teaching statistics in medical schools. The layout of the program is based on the principles of hypertext structure. Also interactive features, illustrative graphs, and figures are provided. The main advantage of the program, from the student's point of view, is that it is tailored according to the curriculum the students are supposed to cover within the first year in the course Biophysics and Biostatistics. Besides the chapters explaining the main ideas and definitions, certain parts beyond the basic knowledge are included. These parts are not mandatory but their purpose is to give more precise explanations to those who are interested.

The program provides a fulltext lookup feature to help the reader to find a specific material. A glossary is available to improve on the search ability.

These and other features of the program were made possible by the Authorware Professional 5.1 system.

The project was supported by a grant from the Ministry of Education (1852/F3/00).

Address for correspondence: I. Krulichová, Dept. of Biophysics, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Electrophysiological diagnostics of neuro-psychiatric disorders and objective evaluation of their treatment

Grant Agency: Ministry of Health

Project Number: 4800-3/98

Principal Researcher: Miroslav Kuba

Joint Researchers: František Vít, Jan Kremláček, Zuzana Kubová, Gerhard Waberžinek, Eva Libigerová, Jana Szanyi, David Gayer

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1122000

Summary of 2000 results

Title of the presentation: Visually evoked cognitive potentials (P300) - characteristics and practical use

Authors: Miroslav Kuba, Jan Kremláček, Jana Szanyi, Jana Chlubnová, Zuzana Kubová (1), František Vít, David Gayer, Gerhard Waberžinek (2), Eva Libigerová (3)

Charles Univ. in Prague, Faculty of Medicine in Hradec Králové, CZ: Depts. of Pathophysiology, Physiology (1), Neurology (2) and Psychiatry (3)

As a part of our research oriented toward a diagnostic use of the electric brain activity analysis during processing of visual information, we tested also an informative contribution of cognitive (event related) potentials when compared to primary visual evoked potentials (VEPs) - pattern reversal VEPs generated in the striate area - and to secondary motion-onset related VEPs from medio-temporal associate cortex. The cognitive task - recognition of non-coherent (target stimulus) vs. coherent (frequent stimulus in "oddball paradigm") motion (used in 30 healthy subjects, in a group of 26 migrenous patients and in a group of 30 patients with anxious-depressive states) produced dominant P300-like positivity with maximum located at Cz (in majority of subjects). Although both groups of patients displayed some cognitive deficit according to average parameters of P300, there is a large overlapping of their values with those in the control group. The large inter-individual variability of P300 latencies (var. coef. 13.2%) limits their use for evaluation of intraindividual changes. This was confirmed in our study of the effect of alcohol. Moreover, it was evident that better objective evaluation of cognitive function can be achieved with the use of negative peak preceding the P300 which has lower variability and displays higher sensitivity to the tested alcohol and drug effects in comparison to primary VEPs. Manipulation with some other variants of cognitive visual stimuli has shown that simplification of the cognitive task can reduce variability of the event related potentials the latencies of which did not correlate with the simultaneously recorded reaction time.

Supported by the Czech Ministry of Health, Grant No. 4800-3/98

Address for correspondence: E - mail: kuba@lfhk.cuni.cz

Title of the research project: Electrophysiological assessment of human cognitive processes

Grant Agency: J. S. McDonnell Found., USA **Project Number:** 99-57EE

Principal Researcher: Miroslav Kuba

Joint Researchers: Jan Kremláček, Zuzana Kubová, Colin Blakemore, Philip Benson

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1983000

Summary of 2000 results

Title of the presentation: Cognitive component in visually evoked event related cortical potentials

Authors: Miroslav Kuba, Jan Kremláček, Jana Szanyi, Jana Chlubnová, Zuzana Kubová (1), František Vít, David Gayer

Charles Univ. in Prague, Faculty of Medicine in Hradec Králové, CZ: Depts. of Pathophysiology and Physiology (1)

There is a generally accepted view that the P300 peak in event-related brain evoked potentials represents a cortical activity reflexing cognitive process. However, from our experiments with simultaneously recorded cortical evoked potentials and reaction time to the target visual stimuli (in "oddball paradigm"), it is evident that the relationship between P300 latency and the mean reaction time is individually very different and that in majority of subjects the P300 latency is longer than the mean reaction time. The large variability in the correlation between these parameters indicates possibly different individual brain strategy in solving the cognitive task with subsequent reaction to the target stimuli. The data obtained in a group of 36 healthy subjects show that the cognitive process is more likely represented by the negative peak preceding the P300, the latency of which is much more constant (its variation coefficient in some variants of cognitive stimuli is about comparable with that of primary visual evoked potentials).

Supported by James S. McDonnell Foundation for Cognitive Neurosci., USA,
Grant No.99-57EE-GLO.04.

Address for correspondence: E - mail: kuba@lfhk.cuni.cz

Title of the research project: The importance of effective atrial contraction for sequential pacing

Grant Agency: Ministry of Health

Project Number: NA/5403-3

Principal Researcher: Jiří Kvasnička

Joint Researchers: Miroslav Měšťan, Vladimír Rozsival, Miloslav Tauchman, Zdeněk Tušl, Alena Štrasová, Karla Dominiková, Pavel Rejchrt, Jakub Střítecký, Vratislav Dědek, Miloš Táborský

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 308000

Summary of 2000 results

Title of the presentation: Atrial contribution and its influence on pacing mode choice

Authors: Miroslav Měšťan (1), Jiří Kvasnička (1), Alena Štrasová (2), Karla Dominiková (3), Vratislav Dědek (4), Jakub Střítecký (1), Zdeněk Tušl (1)

Faculty Hospital, Charles University, Hradec Králové: Department of Internal Medicine (1), Department of Haematology and Oncology (2), Department of Cardiovascular and Pulmonary Diagnostic (3); District Hospital, Ústí nad Orlicí (4)

Atrial contribution (AC) to ventricular filling is not a common parameter for setting of pacemakers used at cardiology departments, mainly because it is not easy to quantify. We have developed a new method for AC measurements using the pulse oximetry saturation signal. One of the aims of our research is to establish a reproducibility of this method. If it proves to be acceptable, we will explore the clinical usefulness of the AC measurement for choosing the optimal pacing mode (sequential or ventricular pacing (VVIR)). Since the beginning of the study in 1999, 18 patients with DDDR pacemakers have been enrolled. In one patient, it was not possible to measure the AC because of irrepressible ventriculoatrial conduction – a newly found limitation of the AC measurement method. So far, we have proved a negative relationship between AC magnitude and “decreased circulatory filling” (achieved by diuretics), which has been suspected in the past, but has not yet been proved. Reproducibility of values of optimal AV delay obtained from measurements within a time period of about 20 hours is $r=0,789$ for $N=17$. Reproducibility of values of the AC is $r=0,91$ for $N=17$. These results suggest good reproducibility and clinical usefulness for both AC estimation and AV delay optimization. Three adverse events (AE) have been recorded since the beginning of the study. Clinical signs of systemic congestion have been found in two and the pacemaker syndrome in one – all three in patients paced in the VVIR mode.

Project was supported by the Ministry of Health Grant Agency, No NA/5403-3

Address for correspondence: J. Kvasnička, Ist Dep. of Internal Medicine, Faculty Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Influence of intraocular lens's transparence on diferential ability of the eye

Grant Agency: Czech Republic

Project Number: 309/00/D056

Principal Researcher: Hana Langrová

Joint Researchers: Dagmar Hejcmanová

Starting date: 1.9.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 707000

Summary of 2000 results

Title of the presentation: Influence of intraocular lens's transparence on diferential ability of the eye

Authors: Hana Langrová, Dagmar Hejcmanová

Charles University in Prague, Faculty of Medicine in Hradec Králové, Dept. of Ophthalmology

We objectivize and quantificate patient's subjective complains in conditions of lower contrasts and under glare: 1) by patients with initially reduced transparence of the intraocular lens (early cataract) with the visual acuity 6/9 and better on normally used Snellen optotype charts and 2) by cataract patients after implantation of the various types of intraocular lenses (polymetyl-metacrylate, silicone) and 3) by patients after YAG laser capsulotomy because of postoperative clouding of the lens's capsule (secondary cataract). We examine contrast sensitivity on Ginsburg's charts and on a computerized system of the Contrast sensitivity 8010 type and visual acuity using the normalized charts with Landolt rings, all methods without and under glare of 1360,4 cd/m², 342,6 cd/m² and 41,1 cd/m² which is produced by Brightness Acuity Tester.

In the period from September till Dezember 2000: 1) we have prepared validate questionnaire regarding the visual functions of patients, 2) we examined the age-matched control group, 3) we examined 20 patients after YAG laser capsulotomy because of secondary cataract and now we will evaluate their visual functions after surgery with the preoperative one's and with the age-matched control group.

Address for correspondence: MUDr. Hana Langrová, Ph. D, Oční klinika FN, Sokolská 1, 500 05 Hradec Králové

Title of the research project: The detection of residual disease after high-dose therapy in multiple myeloma

Grant Agency: Ministry of Health

Project Number: 4535-3

Principal Researcher: MUDr. Vladimír Maisnar

Joint Researchers: prof. MUDr. Ladislav Chrobák, CSc., prof. MUDr. Jaroslav Malý, CSc., doc. MUDr. Jan Krejsek, CSc., MUDr. Miloslav Kmoníček, RNDr. Ctirad Andrýs

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 806000

Summary of 2000 results

Title of the presentation: The new prognostic factors in diagnosis of multiple myeloma

Authors: Vladimír Maisnar (1), Miroslava Toušková (2), Jaroslav Malý (1), Jan Krejsek (2), Miloslav Kmoníček (1)

Dept. of Clinical Hematology (1) and Institute for Clinical Immunology and Allergy (2), Charles University Teaching Hospital, Hradec Králové, Czech Republic

Currently there are numerous studies looking for prognostic markers in multiple myeloma (MM), because some routinely used predictive factors of response to conventional treatment lost their importance after introduction of high-dose strategies. New, reliable predictors of risk are required to define optimal treatment strategy in individual patients. We have focused on the investigation of prognostic factors related to proliferative activity of neoplastic cells. Forty patients with new diagnosis of monoclonal gammopathy were included in the study.

Among the investigated parameters, determination of the number of circulating myeloma cells appears to be the most promising. Three-color flow cytometry was used to detection of myeloma cells in peripheral blood. For the phenotyping, the following combination of antigens see to be most reliable: CD38/CD45/CD138, CD38/CD54/CD56 and CD54/CD56/CD138. Cell-cycle analysis of the CD38+ cells in the bone marrow may be helpful in differential diagnosis of monoclonal gammopathies. We use DNA labeling by propidium iodide because of better sensitivity compared with classical labeling index. Serum concentration of interleukin-6 and interleukin-1beta correlate with disease activity only in some patients and are of little practical use. The determination of soluble interleukin-2 receptor has also not proved to be useful in multiple myeloma diagnosis.

Project was supported by the Ministry of Health Grant Agency, No. 4535-3.

Address for correspondence: MUDr. Vladimír Maisnar, Department of Clinical Hematology, Charles University Teaching Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Pathogenesis, diagnosis and therapy of malignant diseases.

Grant Agency: Ministry of Education

Project Number: CEZ:13/98.1

Principal Researcher: Jaroslav Malý

Joint Researchers: Jan Pechl , Emil Rudolf , Miroslav Červinka , Zdeněk Fiedler , Vladimír Geršl(2), Michaela Adamcová , Milan Rešl , Pavel Jandík , Zbyněk Vobořil , Jan Bureš , Marcela Kopáčová , Jiří Horáček , Alice Poznarová , Jaroslav Malý , Martin Blažek , Bohuslav Melichar , Pavlína Králíčková , Miroslav Kmoníček , Pavel Žák , Ladislav Jebavý

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 5400000

Summary of 2000 results

Title of the presentation: Pathogenesis, diagnosis and therapy of malignant diseases.

Authors: Jan Pechl (1), Emil Rudolf (1), Miroslav Červinka (1), Zdeněk Fiedler (1), Vladimír Geršl(2), Michaela Adamcová (3), Milan Rešl (4), Pavel Jandík (5), Zbyněk Vobořil (5), Jan Bureš (6), Kopáčová (6), Jiří Horáček (6), Alice Poznarová (6), Jaroslav Malý (6), Martin Blažek (6), Bohuslav Melichar (6), Pavlína Králíčková (7), Miroslav Kmoníček (6), Pavel Žák (7), Ladislav Jebavý(7)

We evaluated the first results on the field of the carcinoma cell lines, cardiotoxicity and nephrotoxicity of cytostatics, effect of topoisomerase for diagnostic criteria of atypical carcinoids, hemostatic changes during stem cell transplantation and results of non myeloablative transplantation regimen.

In vitro Matrigel invasion assay was used for comparison of invasiveness of five stabilized cell lines. Human colorectal carcinoma cell lines (SW420, SW 480) were selected as the models for future experiments. I.v. administration of the new antineoplastic agent Oracin in rabbits in vivo shows no signs of cardiofoxicity. Fifty-four pulmonary carcinoid tumors of surgically treated patients were diagnosed according to histological criteria . The topoisomerase II-alpha is a marker giving a valuable information for diagnostic approach of pulmonary typical and atypical carcinoids. The clinical course of 105 patients admitted for hematopoietic stem cell transplantation to treat a variety of malignancies was monitored. Hemostatic changes were evaluated. Our data shows that D dimers level was elevated and antithrombin level was lower in patients with serious complications of transplantation. The effectiveness of regional chemotherapy was evaluated in patients with metastatic liver involvement of colorectal cancer and malignant melanoma. The activity of systemic oxaliplatin in combination with 5-fluorouracil and leucovorin was also studied in patients with metastatic colorectal cancer. . Two patients with multiple myeloma, four with non Hodgkin lymphoma, one patient with aplastic anemia and one patient with Grawitz tumour were transplanted with minimal conditioning (Flu/Cy) and peripheral blood .

Project was supported by the Ministry of Education grant No CEZ -MŠMt 11500002

Address for correspondence: J. Malý, Dept. of Medicine, Charles Univ. in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Rep.

Title of the research project: Fluid balance and neuromuscular disorders in critical illness

Grant Agency: IGA

Project Number: NB51-97/3

Principal Researcher: Jan Maňák

Joint Researchers: Maňák J., Schreiber M., Kunc P, Matulová H., Havel E, Cerman J. Pára F. , Sobotka L., Zadák Z.

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 556000

Summary of 2000 results

Title of the presentation: Acute weakness in the ICU – electrophysiological and pathological findings

Authors: Maňák J., Lukáš Z., Schreiber M., Kunc P, Matulová H., Pára F. , Sobotka L., Zadák Z.

Objective: To describe electrophysiological and histopathological findings in patients with acute weakness which developed in the ICU .Material and methods: All patients with clinical signs of acute onset quadraparesis were studied prospectively. In 9 critically ill patients of mean age 55 (21 – 78) years, clinical examination, electrophysiological studies and skeletal muscle biopsies were performed. Results: Clinical examination: all of our patients had signs of quadraparesis and generalized hypo- or areflexia of tendon reflexes and prolonged dependence on the ventilator. Electrophysiology: Compound muscle action potentials were markedly reduced (mean 18+15% of normal values) or totally absent in all patients. Sensory nerve action potentials were reduced or absent in 6 patients, only 2 patients had normal SNAP. Nerve conduction velocities were normal or slightly reduced .Needle electromyography showed fibrillations and positive sharp waves in 8 patients. No pathology in repetitive stimulation was found. Histopathology: all skeletal muscle biopsies showed pathologic alterations. Fibre diameters varied from atrophy to normal. Internal nuclei, fibre splitting and focal regressive changes with increased activity of lysosomal acid phosphatase were found. In 50% of cases regenerating fibres were present. Endomysial fibrosis was common. All the changes were classified as myogenic, no convincing signs of neurogenic atrophy were noticed. One patient revealed disuse atrophy. Conclusions: We found electrophysiologic signs of axonal sensory-motoric polyneuropathy in all our patients. In spite of that, no neurogenic changes in the muscle were found in the biopsies, the changes in skeletal muscles had a myopathic pattern. These data suggest, that in acute quadriplegia of the critically ill , both the nerve and the muscle are affected simultaneously.

Address for correspondence: Jan Maňák, Dept. Metabolic Care, University Hospital Hradec Králové, 50000 Czech Republic

Title of the research project:

Effect of corticoliberin on secretion of pituitary hormones.
Pharmacological treatment of pituitary tumours by apoptosis inducers in vitro.

Grant Agency: Charles University**Project Number:** 279/98 C**Principal Researcher:** MUDr. Martina Mareková**Joint Researchers:**

Doc. MUDr. Jaroslav Cerman, CSc.
MUDr. Viktor Bartanusz, CSc.
Mgr. Renata Köhlerová

Starting date: 1.1. 1998**Duration (years):** 3**Funds allocated for project - total in Czech crowns:** 730000**Summary of 2000 results****Title of the presentation:** Hypericin inhibits cellular growth of AtT20/D16v-F2**Authors:** Martina Mareková (1), Jiřina Vávrová (2), Doris Vokurková (3), Jaroslav Cerman (1).

(1) Department of Medical Biochemistry, Charles University in Prague, Faculty of Medicine in Hradec Králové,

(2) Institute of Radiobiology and Immunology, Purkyně Military Medical Academy, Hradec Králové

(3) Institute of Clinical Immunology and Allergology, University Hospital, Hradec Králové

Cultivation with 4-8 mmol/l hypericin (specific protein kinase C inhibitor) activated by light induced high inhibition of the rate of HL-60 cell (human promyelocyte leukemia) growth. When hypericin treated cells were not exposed to light growth inhibition was insignificant. Cultivation with light activated hypericin in concentration 16 mmol/l slightly inhibited growth rate of AtT20/D16v-F2 cells. AtT20/D16v-F2 cells did not proliferate in presence of light activated 32 mmol/l hypericin. Evidence of apoptosis was found in HL-60 cells treated with 1-8 mmol/l light activated hypericin, with maximum of apoptotic cells detected after 8 mmol/l light activated hypericin. Light activated hypericin induces both apoptosis and necrosis in dose and time dependent manners in HL-60 cells, but causes only necrosis in AtT20/D16v-F2 cells.

Acknowledgement: Charles University, grant No. 279/98 C, and partly Ministry of Education, grant No. MSM 111500001, supported this work.

Address for correspondence: M. Mareková, Dept. of Biochemistry, Charles Univ., Faculty of Medicine, Šimkova 870, 500 01 Hradec Králové, Czech Rep., marekova@lfhk.cuni.cz

Title of the research project: Innovation of Medical Curriculum

Grant Agency: Ministry of Education

Project Number: MS111500005

Principal Researcher: prof. PhDr. Jiří Mareš, CSc.

Joint Researchers: doc. MUDr. Věra Hubková, CSc., doc. MUDr. Alena Stoklasová, CSc., prof. MUDr. RNDr. Miroslav Červinka, CSc., doc. MUDr. Zuzana Červinková, CSc., prof. MUDr. Ivo Šteiner, CSc., prof. MUDr. Jiřina Martínková, CSc., doc., MUDr. Jindra Šmejkalová, CSc., doc. MUDr. Yvona Mazurová, CSc., doc. MUDr. Jaroslav Mokřý, doc. MUDr. Antonín Hlava, CSc., doc. MUDr. Jan Vokurka, CSc., doc. MUDr. Vladimír Palička, CSc., doc. MUDr. Danuše Šubrtová, CSc., MUDr. Olga Procházková

Starting date: 1.1.1999

Duration (years): 5

Funds allocated for project - total in Czech crowns: 844000

Summary of 2000 results

Title of the presentation: Innovation of Medical Curriculum

Authors: Jiří Mareš, Fac. Med., Charles Univ., Hr. Králové: Dept. Social. Medicine

Faculty level: The Project of Innovation of Dentistry Curriculum has been both finished and approved of by academical authorities for academical year 2000/2001. The core of the innovation: preservation of curriculum duration (5 years), increase in dentistry disciplines up to 50% in the whole curriculum, reinforcement of aspects of dentistry in other non-related disciplines, strong emphasis on the practical part of the study in accordance with the requirements of EU. This project, which could be termed as outcome-based curriculum, was also presented at several conferences abroad.

International level: A lot of analytical and comparative work with the data from documents and internet resources based on the international experience with innovation of medical curriculum have been done. Also many visits have come about at Universities in different countries such as Maastricht (the Netherlands), Coimbra (Spain), Saarlandes (Germany). Intensive international exchange has occurred in the field of pharmacology with significant participation of The Department of Pharmacology.

Transdisciplinary level: Several studies have been accomplished:

1. Evaluation of students' opinion on quality of instruction in all subjects and their suggestions on the innovation. 2. Inquiry of graduate students' opinion on the quality of instruction and clinical training. 3. Study focused on analysis of the hidden curriculum phenomenon at Faculty of Medicine. 4. Evaluation of students' preparation for work with ethnic minorities.

Department level: Innovation in teaching of the following subjects: anatomy, histology, embryology, biology and genetics, physiology, pathological anatomy, pharmacology, radiology, otorhinolaryngology, preventive medicine and hygiene. Innovation is pursued by fundamental innovation of practical part of education, use of electronic interactive tools etc.

Address for correspondence: J. Mareš, Dept. of Social Medicine, Charles University Faculty of Medicine Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Population modelling of wanted and unwanted clinical outcome or surrogate parameters.

Grant Agency: Ministry of Education

Project Number: 37932

Principal Researcher: Jiřina Martínková

Joint Researchers: Jaroslav Chládek (1), Milan Grundmann, Hana Brozmanová, Blanka Kořístková (2), Jiří Grim (1), Marie Šimková, Jaroslava Vaněčková, Vlasta Koudelková, Marie Nožičková (3), Jan Starý (4), Jiřina Chládková, Jiří Hak, Eva Pařízková (5)

(1) Dept. of Pharmacology, (3) Dept. of Dermatology, (5) Dept. of Pediatrics, Faculty of Medicine in Hradec Králové, (4) Dept. of Pediatrics, 2-nd Faculty of Medicine in Prague

Starting date: 1.1.1999

Duration (years): 5

Funds allocated for project - total in Czech crowns: 3000000

Summary of 2000 results

Title of the presentation: POPULATION PHARMACOKINETICS OF CARBAMAZEPINE IN PATIENTS WITH EPILEPSY

Authors: J. Chládek, M. Grundmann, H. Brozmanová, B. Kořístková, J. Martínková
Department of Pharmacology, Faculty of Medicine, Charles University, Hradec Králové,
Department of Clinical Pharmacology, Hospital in Ostrava, Czech Republic

The population pharmacokinetics of carbamazepine (CBZ) in patients with epilepsy were investigated with the help of NONMEM version V 1.1 (Sheiner et al. Am Statistician 1980; 34:118-119). The factors evaluated for their possible effect on the apparent oral clearance of CBZ (CL) were: total body weight (TBW), age, sex, and concomitant treatment with valproic acid (VA), primidone (PRIM) or phenytoin (PHE).

A total of 758 steady-state CBZ serum concentrations were obtained in 604 patients (329 female and 275 male) treated with CBZ in monotherapy (N=333) or with CBZ in combination with VA (N=167), PRIM (N=28) or PHE (N=76). The pharmacokinetics of CBZ was described using a one-compartment model with first-order absorption and elimination. The rate constant of absorption was set at 0.055 h⁻¹ and the ratio of the volume of distribution and bioavailability to 1.8 l.kg⁻¹. The final regression model obtained using the first order conditional estimation method was:

CL (l. h⁻¹. kg⁻¹)=0.36 . TBW^{-0.56}. VAL^{1.19}. PRIM^{1.81}. PHE^{1.54}.

The results show that CL of CBZ exponentially decreases with TBW which was a better predictor of CL than was age. Concomitant administration of VA, PRIM or PHE resulted in an increase in CBZ clearance by 19±5%, 77±29%, and 51±8%, respectively. There was no inter-sexual difference in CL of CBZ

Address for correspondence: Jaroslav Chládek, Department of Pharmacology, Faculty of Medicine, Charles University, Hradec Králové

Title of the research project: Neural transplantation into experimental model of Huntington's disease.

Grant Agency: Ministry of Health

Project Number: 5400-3/99

Principal Researcher: Doc. MUDr. Yvona Mazurová, CSc.

Joint Researchers: RNDr. Věra Valoušková, CSc., Prof. MUDr. Josef Špaček, DrSc.

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 829000

Summary of 2000 results

Title of the presentation: Experimental model of Huntington's disease: Interrelationship between the ibotenic lesion, neural transplantation and subventricular zone within the rat brain.

Authors: Mazurová Yvona (1), Valoušková Věra (2), Špaček Josef (3)

Charles Univ., Fac. Med. in HK: Dept. Histol. Embryol. (1), The Fingerland Dept. Pathol. (3); Acad. Sci. - Inst. Physiol., Prague (2)

The standardization of the ibotenic acid (IA) lesion, which is used as a model of neurodegenerative changes in the brain of Huntington's diseased patients, was finished. It was followed by transplantation (TR) of fetal neostriatum in approx. half of the animals (34 rats). Until now the material was taken from 2 groups of rats (of 14 days and 1 month survival). The characteristics of this lesion and graft were compared with our previous findings concerning the kainic acid lesion, followed by TR. We also began with the evaluation of the proliferating activity of the subventricular zone (SVZ) in lateral brain ventricles in relation to the above-mentioned interventions. These preliminary results showed that the proliferation within the SVZ was higher in relation to IA lesion and that the majority of these generating cells were GFAP-positive astrocytes. Our findings in TR animals were not so explicit – the influence of different conditions must be discussed and the continuation of the study with larger group of animals is necessary.

Project is supported by Ministry of Health Grant Agency of the Czech Republic, No. 5400-3.

Literature: Namiki, J. and Tator, Ch. H.: J. Neuropathol. Exp. Neurol. 58 (1999) 489-498

Address for correspondence: Y. Mazurová, Dept. Histol. Embryol., Charles Univ. in Prague, Fac. Med. in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Republic

Title of the research project: Adoptive immunotherapy as a part of the combined treatment of liver metastases

Grant Agency: Ministry of Health

Project Number: 4676-3

Principal Researcher: Bohuslav Melichar

Joint Researchers: Miroslava Toušková, Pavel Jandík, Jindřiška Mergancová, Zbyněk Vobořil, Otakar Kopecký, Jan Krejsek, Eva Burešová, Jan Bureš, Václav Derner

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 840000

Summary of 2000 results

Title of the presentation: Adoptive immunotherapy by hepatic arterial administration of activated mononuclear cells in patients with liver metastases

Authors: Bohuslav Melichar, Miroslava Toušková, Milan Bláha, Pavel Veselý, Josef Dvořák, Jaroslav Cerman, Pavel Jandík, Jindřiška Mergancová, Zbyněk Vobořil

Liver is the most common site of metastatic disease. Our experience indicates that regional chemotherapy in patients with colorectal cancer, biliary tract carcinoma or malignant melanoma leads to objective response and long term survival in many patients, but almost all patients with non-resectable liver metastases ultimately die of cancer. We have shown that significant proportion of patients with liver metastases present with decreased CD4+ and CD8+CD28+ lymphocytes and that current therapeutic regimens, including irinotecan alone or in combination with 5-fluorouracil, doxorubicin/paclitaxel or regional chemotherapy significantly increase the number of CD4+ and CD8+CD28+ lymphocytes. We investigated the feasibility of hepatic arterial infusion of autologous mononuclear cells alone, or in combination with intraarterial melphalan. The monocytes were harvested by leukapheresis after priming with GM-CSF or interleukin-2 (IL-2) in patients with liver metastases progressing after at least 2 lines of chemotherapy or biologic therapy. Usually more than 2×10^{10} cells (about 50 % monocytes) were obtained by leukapheresis. The cells were activated by IL-2, GM-CSF and interferon-g, and cultured overnight or for 2 hours. An increase in the number of CD14+CD38+ and CD13+CD33+ cells was observed during the overnight culture. The activated mononuclear cells, which exhibited some cytotoxicity, were infused via a catheter into the hepatic artery. Except for a grade II. fever in all patients, the infusion was well tolerated. A 50 % decline of serum carcinoembryonic antigen levels was observed in one patient. In conclusion, many patients with liver metastases present with immunodeficiency which is improved by chemotherapy. Hepatic arterial administration of adoptive immunotherapy represents a potential strategy for consolidation or salvage treatment in these patients.

Address for correspondence: Bohuslav Melichar M.D., Ph.D. Department of Oncology and Radiotherapy, Charles University Medical School and Teaching Hospital, Hradec Králové

Title of the research project: Characterization of differentiation potential of neural stem cells

Grant Agency: Czech Republic

Project Number: 304/00/0338

Principal Researcher: Doc. MUDr. Jaroslav Mokrý, Ph.D.

Joint Researchers: MUDr. Jana Karbanová, Prof. MUDr. Stanislav Němeček, DrSc., MUDr. Miloslav Uher, Ing. Jaromír Lukáš, CSc., RNDr. Věra Palečková

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1465000

Summary of 2000 results

Title of the presentation: Analysis of neural stem cells: Phase I

Authors: Jaroslav Mokrý, Jana Karbanová

Department of Histology and Embryology, Charles University Medical Faculty, Hradec Králové

Initial phase of the project was aimed at optimization of procedures yielding the highest numbers of neural stem cells (NSCs). An aggregation culture for cultivation of EGF- and FGF-2-derived neurospheres was adopted as routine method permitting isolation and expansion of NSCs from rat and mouse fetal brains. To assess differentiation potential of harvested NSCs, cells were isografted either into the intact brain of experimental animals (in the form of neurospheres or as dissociated cells) or injected in the tail vein of irradiated Balb/c mice. Experimental animals were left to survive for several months; tissues of interest will be processed for histology in the next phase of the project. To allow a precise identification of grafted cells, NSCs were transfected in vitro with lacZ gene using a retroviral vector. Different batches, doses and schemes for transfection (e.g. successive administration) were used to find out optimum conditions. Effectiveness of the labelling was evaluated after staining with X-Gal which detects the enzymatic activity of exogenous beta-galactosidase. Although the detection enabled us to identify the whole clonal progeny derived from labelled NSCs, the percentage of labelled cells was low (1-5%), which dictates the need to seek for a more efficient labelling method. Another part of the study was focused on NSCs residing within the subependymal zone (SEZ). Using immunohistochemical detection of proliferation markers, we tested proliferative response of NSCs in the SEZ to variety of stimuli inducing injury of the brain tissue. This subsequently initiates endogenous repair via activation of endogenous NSCs. Neurotoxic sodium nitroprusside and kainic acid were recognised as the most potent activators of NSCs since they induced the highest and earliest response in SEZ cells.

Supported by Grant Agency of the Czech Republic, No. 304/00/0338

Address for correspondence: Doc. MUDr. Jaroslav Mokrý, Ph.D., Department of Histology and Embryology, Charles University Medical Faculty, Šimkova 870, 500 01 Hradec Králové

Title of the research project: Encapsulation of neural mammalian cells for treatment of neurodegenerative diseases

Grant Agency: Czech Republic

Project Number: 304/98/267

Principal Researcher: Ing. Jaromír Lukáš, CSc.

Joint Researchers: Doc. MUDr. Jaroslav Mokrý, Ph.D., Doc. MUDr. Karel Smetana, DrSc.

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2137000

Summary of 2000 results

Title of the presentation: Biological properties of new copolymers designed for cell encapsulation

Authors: Jaroslav Mokrý (1), Jana Karbanová (1), Jaromír Lukáš (2), Věra Palečková (2)
Dept. Histol. Embryol., Charles University Medical Faculty, Hradec Králové (1), Inst. Macromol. Chem., Acad. Sci. Czech Rep., Prague (2)

Allo- and xenogeneic cells releasing bioactive compounds (neurotransmitters, trophic factors, hormones, endorphins etc.) could be utilised in therapy provided that they had been encapsulated with semipermeable membrane which will protect induction of immune response. Novel synthetic hydrogels were prepared and their physical, chemical and biological properties were tested. Of these, HEMA-EMA, HEMA-IPMAAm and HEMA-tBMAAm copolymers were chosen for encapsulation experiments. The principal investigator constructed microencapsulation apparatus in the Tissue Culture Laboratory in the Department of Histology and Embryology. HEMA-IPMAAm that produced transparent but sticky capsules was excluded from experiments because of difficult processability. Microcapsules from 2 remaining hydrogels were implanted into the rat brains that were allowed to survive for ½–6 months. Histological examination was focused on cellular response (macrophages, foreign body giant cells, microglia, reactive astrocytes) and connective tissue elements (collagen and reticular fibres). Our results demonstrated that HEMA-EMA copolymer was well tolerated and did not induce irritation of the brain tissue (for detailed description see reference below). Transparent HEMA-IPMAAm copolymer was used for encapsulation of PC12 cells since its transparency enabled us to directly visualise entrapped cells. These capsules were implanted into brains of mice and rats; after processing for histology, examination will be concentrated on evaluation of tissue response to implants and extent of reaction will be compared with reaction induced by capsules not containing cells.

Supported by Grant Agency of the Czech Republic, No. 304/00/0338

J. Mokrý, J. Karbanová, J. Lukáš et al.: Biocompatibility of HEMA copolymers designed for treatment of CNS disease with polymer-encapsulated cells. *Biotechnol Prog* 16, 2000, 897-904.

Address for correspondence: Doc. MUDr. Jaroslav Mokrý, Ph.D., Department of Histology and Embryology, Charles University Medical Faculty, Šimkova 870, 500 01 Hradec Králové

Title of the research project: Reactive oxygen species in pathogenesis of acute pancreatitis and antioxidative treatment.

Grant Agency: Ministry of Health

Project Number: NB/6043-3

Principal Researcher: František Musil

Joint Researchers: Zdeněk Zadák, Luboš sobotka, Dagmar Solichová, Jan Maňák, Milan Kaška

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 417000

Summary of 2000 results

Title of the presentation: Reactive oxygen species in pathogenesis of acute pancreatitis and antioxidative treatment.

Authors: František Musil (1), Zdeněk Zadák (1), Luboš sobotka (1), Dagmar Solichová (1), Jan Maňák (1), Milan Kaška (2)

Teaching Hospital, Charles University, Hradec Králové Department of Gerontology and Metabolic Care (1), Department of Surgery (2)

Objectives: 1. To evidence enhanced activity of reactive oxygen species (ROS) in the course of acute pancreatitis (AP) by evaluation of plasmatic markers of activity of ROS.
2. To evaluate dynamics of plasmatic markers of activity of ROS and dynamics of plasmatic concentrations and activities of antioxidants.
3. To compare dynamics of markers of activity of ROS and dynamics of activities and concentrations of antioxidants in patients suffering from AP with dynamics of markers of activity of ROS and dynamics of activities and concentrations of antioxidants in patients with other illnesses located in the abdominal cavity.

Results: Blood samples from a group of 10 patients with AP were analysed on admission, 4th and 8th day of hospitalisation. We found these results:

1/ significant increase of serum concentration of selenium in 8th day against concentration on admission

2/ significant decrease of concentration of selenium in red cells in 8th day against concentration on admission

3/ significant decrease of serum concentration of total vitamin C in 4th and 8th day against concentration on admission

Conclusions: We found significant changes in dynamics of concentrations of several reported antioxidants in the course of AP which might be clinical significance.

But in present time we have not compared these data with data from a control group of healthy persons and a control group of patients with other illnesses located in the abdominal cavity yet to estimate the possible clinical significance.

Address for correspondence: František Musil, Department of Gerontology and Metabolic Care, Teaching Hospital, Charles University, Sokolská 408, 50005 Hradec Králové, Czech Republic

Title of the research project: Analysis of Cataract Surgery Outcomes

Grant Agency: Charles University **Project Number:** 47053

Principal Researcher: Doc. MUDr. Jan Novák, CSc.

Joint Researchers: Prof. MUDr. Pavel Rozsival, CSc.
MUDr. Daniela Nováková
Ing. Josef Kvasnička
Hana Dvořáková

Starting date: 1. 1. 1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 180 000

Summary of 1999 results

Title of the presentation: New database programme for evaluation of cataract surgery outcomes at the Department of Ophthalmology in Hradec Králové.

Authors: Jan Novák, Daniela Nováková, Pavel Rozsival, Josef Kvasnička, Hana Dvořáková, Department of Ophthalmology, Faculty of Medicine, Charles University, Hradec Králové

Aims: To describe and evaluate the basic data of all cataract patients operated at the Department of Ophthalmology in Hradec Králové during 36 months in a prospective study using special newly made database. **Methods:** The data of cataract surgeries were systemically collected and evaluated in the computer database used program Access 7.0 of Microsoft for this purpose. Subjective valuation of the operation results was explored. The questionnaire containing special 14 questions concerning the patient's difficulties before surgery compared with their possible activities after cataract surgery was prepared for this purpose. **Results:** Five surgeons performed 9510 cataract surgeries (9321 primary extractions and 199 /2,09%/ secondary implantations) during this period. 52 % of all them were performed like outpatient surgery. Surgeons used method of parabolbar anesthesia in 45,7% and subtenonal in 51,4%, scleral incision in 70,6%, clear corneal in 29,4% and temporal incision in 11,2% respectively. The tunnel length of more than 5mm was used in 62%, 5mm in 14,2% and less than 5mm in 23,8%. Only 18,6% of wounds were closed with the suture. The anterior capsule was opened using CCC in 95,1%. Method of phacoemulsification was used in 98%. 82 IOL types were used in this period. Only 21,7% of foldable lenses were implanted, but the number increases gradually. The most frequent implanted PMMA IOL was Erika P314A from Ergolens Co. (1339-14%) and C455F from ORC Co. (1320-14%). The most frequent used foldable lens was AcrysofMA60BM (653=6,9%) from Alcon Co. and SI30NB (562=6%) from Allergan Co. The posterior capsule rupture (PCR) was established as the main significant complication of the phacosurgery. PCR varied from 0,97% to 6,38% in the group of 5 surgeons (averidge 1,9%). In the year 1998 and 1999 the database was used for the European Cataract Outcomes Study organized regularly each october. Our surgical and functional results were valuated on the middle level in the group of 30 participants from the Europe. Our program of cataract surgery data evaluation will be used by EriLens Company for wide exploitation at the surgical departments of ophthalmology and a national cataract database in the Czech Republic.

Address for correspondence: Doc. MUDr. Jan Novák, CSc, Department of Ophthalmology, Teaching Hospital, Hradec Králové, Sokolská 1, 500 05, Czech Republic

Title of the research project: Phonosurgical treatment of voice disorders

Grant Agency: Ministry of Health

Project Number: NK/4528-3

Principal Researcher: Ivana Nováková

Joint Researchers: Martin Kučera, Jakub Dršata, Jan Vokurka, Ivan Hybášek, Milan Rešl

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1751000

Summary of 2000 results

Title of the presentation: Functional results of phonosurgical procedures

Authors: Martin Kučera, Jakub Dršata, Ivana Nováková

ENT Dept., University Hospital Hradec Králové

Results of operations at 49 patients treated for incomplete vocal cord closure in the years 1998 - 2000 have been evaluated. Thyreoplasty I. typ by Harries - Morrison was performed in 32 cases - 5 times for vocal cord atrophy, 25 times for unilateral vocal cord paresis, 2 times for laryngeal trauma. Injection of teflon was used in 12 cases - 11 times for vocal cord atrophy, once for unilateral vocal cord paralysis. Injection of Gelfoam was performed 4 times - 3 times for vocal cord atrophy and once for vocal cord paralysis. Postoperative prolongation of maximum phonation time at unilat. vocal cord paralysis was 7 sec., 5 sec. at vocal cord atrophy. Postoperative improvement of maximum intensity range of voice was 6dB at vocal cord atrophy and 14 dB at unilateral vocal cord paralysis. The improvement of frequency scale of the voice was 4 half-tones at vocal cord atrophy and 8 half-tones at vocal cord paresis. 10 patients of 18 with preoperative aspirations showed complete postoperative relief, good improvement occurred in 3 cases and partial relief at 5 cases. The most risk factors for good functional result seem to be spasticity, major neurologic handicap, amusia, old age and preoperative anatomical changes of the larynx.

The project was supported by the Ministry of Health Grant Agency NK/4528-3.

Address for correspondence: Martin Kučera, ORL klinika Fakultní nemocnice, 500 05 Hradec Králové, tel.: 049/583 2173, fax: 049/583 2033, mail: kucermar@seznam.cz

Title of the research project: Interaction of 7-methoxytacrine and galanthamine with potential neuroprotective agents

Grant Agency: Ministry of Health

Project Number: NL/6091-3

Principal Researcher: Vladimír Palička

Joint Researchers: Pavel Živný, Jaroslava Vávrová, Josef Herink, Jiří Bajgar, Jaroslav Květina, Zbyněk Svoboda

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1974000

Summary of 2000 results

Title of the presentation: The influence of 7-methoxytacrine and L-carnitine on brain acetylcholinesterase activity

Authors: Vladimír Palička (1), Pavel Živný (1), Josef Herink (2), Jiří Bajgar (2), Jaroslav Květina (3), Jaroslava Vávrová (1), Zbyněk Svoboda (3)

Faculty of Medicine, Charles University, University Hospital Hradec Králové: Inst. Clin. Biochem. Diagn. (1), Purkyně Medical Academy Hradec Králové: Dept. Toxicology (2), Academy of Science, Inst.Exp.Biopharm. & PRO.MED.CS., Hradec Králové (3)

The new method for total and free carnitine estimation in different biological materials was developed and applied for automatic analyser Cobas Mira (Roche). The main effort was to optimise the measurement conditions and method validation for rat serum, urine and various organ homogenates measurements. The modified method has very high sensitivity; minimal measured concentration is 3 µmol/l, calibration curve is linear to the concentration 800 µmol/l of L-carnitine. Concentrations in rat serum, urine and lung homogenates was within this range.

The aim of second part of this study was to assess the influence of L-carnitine on rat brain acetylcholinesterase inhibition by 7-methoxytacrine in vivo. Changes in acetylcholinesterase activity in the frontal cortex, hippocampus, medial septum and basal ganglia were studied in rats. The animals were separately treated intraperitoneally with L-carnitine and intramuscularly with 7-methoxytacrine, or they were treated for 3-days with different doses of L-carnitine followed by one intraperitoneal administration of 7-methoxytacrine. 7-methoxytacrine differentially inhibited acetylcholinesterase activity in the brain parts. L-carnitine itself did not influence the activity of this enzyme. 3-day treatment of L-carnitine followed by administration of 7-methoxytacrine increased the inhibition of the enzyme in all brain parts studied. When 7-methoxytacrine was administered intracerebroventricularly following 3-day treatment with L-carnitine, the inhibition was less expressed in comparison with systemic administration. Moreover, the inhibition potency in this case was not influenced by L-carnitine.

Project was supported by IGA MZ, No. NL/6091-3

Address for correspondence: V.Palička, Inst.Clin.Biochem.Diagn., University Hospital, Hradec Králové, Czech Republic

Title of the research project: Compendium of laboratory medicine in electronic form

Grant Agency: Ministry of Health

Project Number: 4692-3

Principal Researcher: Vladimír Palička

Joint Researchers: Antonín Jabor, Miroslav Zámečník, Pavel Živný, Miroslav Pecka, Bedřich Friedecký, Jaroslava Vávrová, Jaroslav Masopust

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1454300

Summary of 2000 results

Title of the presentation: Modern electronic form of educational materials in clinical biochemistry

Authors: Vladimír Palička (1), Pavel Živný (1), Jaroslava Vávrová (1), Dana Kakrdová (1), Bedřich Friedecký (1), Antonín Jabor (2), Miroslav Zámečník (2)

Faculty of Medicine, Charles University, University Hospital Hradec Králové: Inst. Clin. Biochem. Diagn. (1), Inst.Postgrad.Med.Education, Dept.Clin.Biochem. Prague (2)

The CD – compendium of laboratory medicine is originally designed to support training and post-graduate education of all categories of scientists working in the field of clinical biochemistry and laboratory medicine. This novel training and educational tool use the multimedial technology to provide library resources of terms and pictures and accompanying text.

Multimedia education tools:

- enable to minimise the difference between clinical and laboratory problems
- integrate knowledge bases of theoretical and clinical subspecialties
- are focused on principles of laboratory methods
- stress knowledge exploration by medical and chemical students
- lead to self-learning skills and independent decision-making
- make good basis for evidence based medicine studies

The wide range of described items cover theoretical aspects of pre-analytical, analytical and post-analytical aspects of measurement, quality management, basic statistical methods, characterization of more than 1500 analytes including various methods of their analysis and finally clinical part with biochemical and pathobiochemical description of organ damage as well as biochemical characterization of common diseases of the particular organ or system.

Project was supported by IGA MZ No. 4692-3

Address for correspondence: V.Palička, Inst.Clin.Biochem.Diagn., University Hospital, Hradec Králové, Czech Republic

Title of the research project: Long term mortality and quality of life after intensive care for critical illness - multicentric prospective study

Grant Agency: Ministry of Health

Project Number: 4530-3

Principal Researcher: Renata Parizkova

Joint Researchers: Renata Parizkova, Vladimir Cerny, Pavel Dostal, Ludek Vasatko, Petr Hora, Ivan Novak, Ivan Herold

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 531 000

Summary of 2000 results

Title of the presentation: Clinical outcome, cost of care and quality of life after intensive care for critical illness in different subgroups of patients: a multicentric study

Authors: Renata Parizkova (1), Vladimir Cerny (1), Pavel Dostal (1), Ludek Vasatko (2), Petr Hora (3), Ivan Novak (3), Ivan Herold (4)

Faculty of Medicine, Charles University Hradec Kralove, Dept. of Anesthesia and Intensive Care (1), Hospital Usti nad Labem, Dept. of anesth. and intensive care (2), Charles University, Faculty Hospital Plzen, Dept. of internal med. (3), Hospital Mlada Boleslav, Dept. of anesth. and intensive care (4)

Intensive care units account for a large proportion of hospital expenditures. The aim of the study was to evaluate different subgroups of patients for clinical outcome, quality of life (SF 36) and cost of care. 1368 patients were prospectively studied. Demographic data, APACHE II and SOFA score, diagnostic group (TR = trauma, TBI = traumatic brain injury, COPD = chronic obstructive pulmonary disease, CPR = cardiac arrest, ARDS = acute respiratory distress syndrome, INTOX = intoxication), length of ICU stay (LOS), clinical outcome, quality of life and cost of care in CZK were recorded. Relationship among, diagnostic groups and severity score were evaluated. Data as mean (SD), median (25-75%), t-test, Mann-Whitney Rank Sum Test, z-test, ANOVA, linear regression (SigmaStat Statistical Software) were used, $p < 0.05$ was considered statistically significant. All patients=Apache II was 24 (8,9), SOFA 8,1 (5,1), mortality 18,9%, TR=115 pts., Apache II 21,8 (8,2), SOFA 8,6 (3,8), mortality 13,9%, TBI group=137 pts., Apache II 23,3 (7,7), SOFA 6,7 (3,3), mortality 10,9%, COPD group=86 pts., Apache II 23,3 (6,8), SOFA 7,1 (3,4), mort. 12,7%, CPR=184 pts., Apache II 32,1 (7,9), SOFA 10,3 (3,4), mort. 28,8%, ARDS=76 pts., Apache II 25,6 (8,1), SOFA 10,7 (3,9), mort. 19,7%, INTOX=425 pts., Apache II 21,2 (8,7), SOFA 7,5 (4,4), mort. 19,5%. There were significant differences among selected groups of patients concerning clinical outcome, cost of care and quality of life. Obtained data may be of great importance in decision making processes, ICU budgeting and comparing different ICUs.

Address for correspondence: Renata Parizkova, Dept. of Anaesth. and Intensive Care, Charles University, Hradec Kralove, 500 05, Czech Republic

Title of the research project: Reconstruction of the Joint Surface using autologous osteochondral Grafts, autologous cultured Chondrocytes in Suspension and in bioactive Glass-Ceramic Material. An experimental and clinical Study.

Grant Agency: Ministry of Health

Project Number: ND/6042-3

Principal Researcher: Jaroslav Pavlata

Joint Researchers: Karel Urban, Pavel Měříčka, Hana Straková, Jindra Brtková, Jan Folvarský,

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1184000

Summary of 2000 results

Title of the presentation: Reconstruction of the Joint Surface.

Authors: Jaroslav Pavlata(1), Karel Urban(2), Karel Karpaš(2), Pavel Měříčka(3), Hana Straková(3), Aleš Kohout(4), Jindra Brtková(5)

Teaching Hosp., Charles Univ., Hr. Králové: Dept.of Othopaedics(1), Dept.of Tissue Bank(3), Dept.of Pathology(4), Dept.of Radiodiagnostic(5), Fac. Med., Charles Univ., Hr. Králové: Dept.of Orthopaedics(2).

Treatment of defects of the joint cartilage is a very much of an orthopaedic problem. The project supposes solution of the treatment of joint cartilage defects by healing through a full-value hyaline cartilage. Recently the new approach to treatment of articular cartilage defects based on use of cultured autologous chondrocytes was introduced to clinical practice. The chondrocytes obtained from uninjured articular cartilage were injected after 14-21 day culture in the form of suspension under the defects that were covered with periosteal flaps. The results of treatment by autologous culture of chondrocytes will be compared with patients who will be treated by the Hangody method in which autologous osteochondral grafts from the zone of cartilage on the femoral condyles which is not in contact with the knee joint movements are transferred to the cartilagenous defects of the knee joint cartilage. Results of these two different methods will be compared by a clinical examination, magnetic resonance, control arthroscopy and biopsy. The experimental part of the project - use of bioactive glass-ceramic material as a carrier of autologous cultured chondrocytes - will form the basis for future research aiming to its use in clinical practice. We carried out cultivation of autologous chondrocytes five times. Transplantation of autologous chondrocytes suspension was used in one patient suffering from a femur condyle defect. Transplantation of osteochondral grafts was carried out in 9 patients. After healing, we did a control arthroscopic examination in 3 patients. The defect was healed by a compact cartilaginous tissue. Bioptic samples were taken from the transplantate in two patients. The microscopic finding consisted of hyaline cartilage (55%) and fibrocartilage (45%).

Project was supported by the Ministry of Health Grant Agency, No: ND/6042-3

Address for correspondence: Jaroslav Pavlata, Charles University Teaching Hospital, Dept. of Orthopaedics, 500 05 Hradec Králové, Czech Republic

Title of the research project: The application of ^{13}C -breath tests in the paediatric clinical practice.

Grant Agency: Ministry of Health

Project Number: NE 6164-3

Principal Researcher: Oldřich Pozler

Joint Researchers: David Neumann, Viktor Voříšek, Jan Bureš, Zdeněk Kokštein, Hubert Vaníček, Petr Dědek

Starting date: 1.4.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 1086000

Summary of 2000 results

Title of the presentation: The investigation of gastric emptying using ^{13}C -octanoic acid breath test in the neonates.

Authors: Oldřich Pozler (1), David Neumann (1), Viktor Voříšek (2), Jan Bureš (3)

University Hospital Hr. Králové, Fac. Med., Charles University, Hr. Králové: Dept. of Paediatrics (1), Dept. of Clinical Biochemistry and Diagnostics (2), Dept. of Medicine (3)

The proper gastric emptying (GE) in premature neonates is an important step to the enteral nutrition management. The ^{13}C -octanoic acid test is a precise tool for the GE measuring, useful in neonates. Octanoic acid (^{13}COA) containing atoms of the carbon ^{13}C stable isotope is finally metabolized as the $^{13}\text{CO}_2$, which is analysed in the exhaled breath. We examine the $^{13}\text{CO}_2/^{12}\text{CO}_2$ ratio in the exhaled breath and the ratio growth illustrates the rate of GE. The analysis is made on Isotope Ratio Mass Spectrometry.

We administered ^{13}COA , added to the pasteurized breast milk, into the stomachs of the 14 stabilised premature neonates (31. - 37. week of gestation, 1400 - 2680g birth weight). We repeated the test 3 times, firstly with a dose below 7 ml/kg/dose, then between 7 to 13 ml/kg/dose and finally 10 to 19 ml/kg/dose of breast milk. Each of the 3 tests were composed of 22 breath samples. We try to find the intra- and interpersonal GE pattern and the rate of GE in tested premature neonates. Results: 1. Each of these neonates has a stable personal GE pattern not depending on the size of the pasteurized breast milk dose. It seems to be genetically determined. 2. There is wide spectrum of normal GE patterns ranging from "quick evacuators" to "slow evacuators". 3. The average $T_{1/2}$ of the GE was 40,3 min. The intrapersonal changes of the GE $T_{1/2}$ were not statistically significant.

Literature: Veereman-Wauters et al: J. Ped. Gastroenterol. Nutr. 1996, 23, 111 - 117

Project is supported by the Ministry of Health Grant Agency, No. NE 6164-3/2000

Address for correspondence: O. Pozler, Dept. of Paediatrics, Teaching Hospital, Hradec Králové, 500 05 Hradec Králové, Czech Republic

Title of the research project: Digital processing of pictorial documentation for topographic dissections and anatomy lectures

Grant Agency: Ministry of Education

Project Number: 1848/2000

Principal Researcher: Olga Rejtarová

Joint Researchers: Dáša Slížová, Otakar Krs

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 337000

Summary of 2000 results

Title of the presentation: Digital processing of pictorial documentation for topographic dissections and anatomy lectures

Authors: Dáša Slížová, Otakar Krs, Olga Rejtarová

Fac. Med., Charles Univ., Hradec Králové, Dept. of Anatomy

Knowledge of topographic anatomy is an essential prerequisite for any physician to be successful in professional career. That is why we pay special attention to topographic dissections completing course of normal human anatomy at our department. Dissection procedure is subjected to relatively rigid rules bringing inevitable problems due to removal of some superficial structures and damage of deeper layers. Thus some important structures get lost for further learning and also for final evaluation of students knowledge and manual skills. Therefore we decided to make an integral system based on digital camera pictures of course of preparation, the topographical situation and unique varieties. From the anatomical point of view, besides recording some very difficult preparations step by step, this camera can make pictures of both synoptical and detailed features of dissected human body. Our further aim has been microphotographic documentation of histological tissue samples from anomalous or accessory organs. For this purpose we have been using microphotographic equipment with digital camera Olympus Camedia C-3030ZOOM. Digital bypassing of the wet photographic process makes the picture processing faster and widens availability of digital pictures through the web. All taken photographs can be further edited, printed, archived on various media, used for instructional, test, evaluative, and publication purposes. With help of digital camera we are able to make our own original pictorial database feasible to be presented at anatomy lectures. From our first experience, we can conclude that nowadays high-end consumer-type digital camera is an invaluable tool for teaching topographic and microscopic anatomy. The opportunity to catch the course of topographic dissections can increase the quality of teaching process.

Address for correspondence: D. Slížová, Dept. of Anatomy, Charles University in Prague, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové, Czech Rep.

Title of the research project: Relationship of capillary vessel count in breast carcinoma to its metastatic potency and prognosis.

Grant Agency: Ministry of Health

Project Number: 4559-3

Principal Researcher: MUDr. Aleš Ryška

Joint Researchers: Prof. MUDr. Ivo Šteiner, CSc., MUDr. Eva Hovorková, MUDr. Pavel Jandík, CSc., MUDr. Vlasta Medková

Starting date: 1. 1. 1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 582000

Summary of 2000 results

Title of the presentation: Angiogenesis in breast carcinoma

Authors: Aleš Ryška, Ivo Šteiner, Eva Hovorková

Faculty Hospital and Faculty of Medicine, Charles University, Dept. of Pathology

Angiogenesis gains increasing attention in recent years, as capillary vessels provide supply of nutrition factors and represent a gate for metastasizing. The aim of the project is: (1) to study number of the capillaries in the tumor and its relationship to the metastatic potency and (2) to analyze the differences in the quantity of the capillaries between tumors with and without previous aspiration biopsy. One hundred and forty two cases of breast carcinoma diagnosed at the Dept. of Pathology, Faculty Hospital, Hradec Králové in years 1997-98 were examined. Endothelial cells were visualized immunohistochemically using antibody against factor VIII (von Willebrand factor). Capillary vessels were counted at 200× magnification (using eyepiece graticule) in the areas of highest angiogenic activity (hot spots) at the periphery of the tumor. The highest microvessel counts (HMC) were correlated with other factors (age, tumor size, grade, nodal status, expression of receptors, proliferative activity, p53, HER-2/neu). The differences between tumors with and without previous aspiration biopsy were analyzed. All patients were women aged 31-86 years (median 59). The size of tumors was 4-70 mm (median 20 mm). Sixty cases have been previously examined by fine needle aspiration cytology; 72 cases were node-positive. The maximum counts of microvessels varied from 26 to 185 (average 63.9, median 60) per microscopic field (area 0.25 mm²). The HMC was significantly higher in node-positive tumors (median 57.5 versus 66; p=0.036). The capillary vessel counts did not correlate with other parameters examined. Fine needle aspiration cytology does not seem to increase the number of intratumoral capillary vessels. We have also compared HMC/mm² in normal breast tissue with those in carcinoma. Interestingly, the values in normal lobules were significantly higher (median 565 vs. 243; p<0.0000001).

Address for correspondence: A. Ryška, Department of Pathology, Charles University Medical Faculty Hospital, CZ-500 05 Hradec Králové, Czech Republic, ryskaale@fnhk.cz

Title of the research project: Introduction of digitally controlled bicycle ergometry in practical classes of physiology.

Grant Agency: Ministry of Education

Project Number: 1854/F3/00

Principal Researcher: Václav Šafka

Joint Researchers: Zuzana Červinková, Lubomír Hadaš

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 120000

Summary of 2000 results

Title of the presentation: Acquisition of exact, digitally controlled ergometry for the practical classes of medical physiology

Authors: Šafka V., Červinková Z, Hadaš L

Topics of several practical laboratory classes of medical physiology deal with reactions and adaptation of the body to physical exercise. Methods used for application of the physical loading are out of date and not enough suitable for the practical demonstration of physiological mechanisms in action. We are trying to improve this situation using digitally controlled bicycle ergometer, which enables exact dosage, measurement and control of the applied physical loading.

- 1) We improve the practical classes of cardiovascular response to physical exercise, where we can replace the old-fashioned Harvard step up test by the actually used test W 170 and other similar tests.
- 2) The practical classes of ECG we can complete by the demonstration of the changes of ECG curve features during physical exercise.
- 3) The practical classes of the impact of physical exercise on diuresis we can improve by application of well-defined physical loading.
- 4) In connection with already available monitor with a probe for continual analysis of respiration gases we can add a new practical demonstration of the raise of oxygen extraction from the inspired air, and, together with added inspired volume measurement, analysis of effectiveness of muscle work.

We believe that this new appliance brings new impulses for the students at our practical classes of medical physiology.

Address for correspondence: Václav Šafka, Dept. of Physiology, Charles University Prague, Medical Faculty H. K., Šimkova 870, 500 01 Hradec Králové, e-mail: safkavac@lfhk.cuni.cz

Title of the research project: Influence of the proportion of the arterial and portal perfusion of the liver on the insulin resistance and liver function in liver cirrhosis.

Grant Agency: Czech Republic

Project Number: 306/99P014

Principal Researcher: Václav Šafka

Joint Researchers: Zuzana Červinková, Petr Hůlek

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 215000

Summary of 2000 results

Title of the presentation: Liver perfusion changes after TIPS and their pathophysiological impact.

Authors: Šafka V., Červinková Z., Hůlek P., Vižďa J., Dufincová J, Fejfar T.

Transjugular intrahepatic portosystemic shunt (TIPS) is a relatively new type of portosystemic side-to-side shunt created by radiological means. This dramatically broadens the indication range of the shunt and asks for new approval of indication criteria. The dramatic change of the liver circulation brings about some typical complications of the shunt - portosystemic encephalopathy and progressive liver failure, the risk of which should be reduced by more accurate indication criteria. A newly studied problem is glucose handling, strongly impaired in cirrhosis. Insulin resistance is usually elevated in a wide range up to overt diabetes, and this condition worsens already not very good prognosis of the patient. By our personal experience, it worsens also the outcome after TIPS. At our hospital, at the 1st Dept. of Medicine, the study of insulin resistance in cirrhotic patients and its development after TIPS has started three years ago. The results appear quite heterogeneous and ask for finding the key influencing factors. We propose that the dramatic change in the liver perfusion after the shunt-creation could be one of them.

We use slight modification of the method of perfusion scan with ^{99m}Tc, published by University of Muenster in 1997, which offers a method to quantify the perfusion changes in the liver.

Up to date, 18 patients undergoing TIPS for diverse reasons were repeatedly investigated using scintigraphic perfusion, euglycaemic clamp and other laboratory analysis and are followed up. The results were presented at two national meetings and we work on refinement of the method of analysis of the scintigraphic data and their correlation with other clinical data. The results of this analysis will be available during the first term of the next year.

Address for correspondence: Václav Šafka, Dept. of Physiology, Charles University Prague, Medical Faculty H. K., Šimkova 870, 500 01 Hradec Králové, e-mail: safkavac@lfhk.cuni.cz

Title of the research project: Clinical Analysis of Osseointegrated Dental Implants with Regard to the Surface Finish of Fixture

Grant Agency: Ministry of Health

Project Number: 4789-3/98

Principal Researcher: Antonín Šimůnek

Joint Researchers: Dana Kopecká, Radek Mounajjed, Zdeněk Strnad

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 3103000

Summary of 2000 results

Title of the presentation: Clinical Analysis of Osseointegrated Dental Implants with Regard to the Surface Finish of Fixture

Authors: Antonín Šimůnek (1), Dana Kopecká (1), Radek Mounajjed (1), Zdeněk Strnad (2)

(1) Charles University in Prague, Faculty of Medicine in Hradec Kralove, Department of Stomatology

(2) LASAK Ltd., Prague

The advantages and disadvantages of hydroxyapatite coated dental implants were studied. Titanium non-coated and hydroxyapatite-coated root-form dental implants were compared. We followed-up:

- Stability of the implants using Periotest.
- Resorption of the peri-implant bone.
- Condition of the peri-implant soft tissue.

1. During the stability test of the implants (n = 54) the results revealed the following: Initial stability of titanium and HA coated implants did not differ. After one-year functional loading the stability of titanium implants was enhanced more than stability of HA-coated implants. Observed changes were statistically significant in all evaluated bone densities (D1-3). No significant correlation, however, was found when individual densities were compared.

2. The resorption of the peri-implant bone was followed by radiovisiography (n = 330). At the end of healing stage there were not significant differences between both groups of the implants. After one year functional loading the resorption didn't exceed 2 mm. In the HA-group the values were significantly lower. After two years functional loading there were not evident differences. During the second year loading the bone resorption in both groups corresponded to the Albrektsson's criterion of success (was less than 0.2 mm).

3. The condition of the peri-implant soft tissue (n = 491) was similar in both investigated groups.

Project was supported by the Ministry of Health Grant Agency, No 4789-3/98.

Address for correspondence: A. Šimůnek, Dept. of Stomatology, Faculty Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Moral Judgement Competence by medical students, measurement and total analysis

Grant Agency: Charles University

Project Number: 296/2000

Principal Researcher: Birgita Slováčková

Joint Researchers: -

Starting date: 29.11.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 41000

Summary of 2000 results

Title of the presentation: Moral competence and moral attitudes of students at the Medical Faculty of Charles University in Hradec Králové

Authors: Birgita Slováčková

University Hospital, Department of Psychiatry

Moral competence is considered as an ability, on the basis of inner principles, to pass moral judgements and to act in accordance with these judgements (in our study, this ability is evaluated by means of the C index). Moral attitudes mainly represent an evaluating relationship partly reflecting rational knowledge, but especially reflecting subjective emotional evaluation of moral problems (in our study, these problems are evaluated by means of 6 stages of moral judgement according to Kohlberg). The aim of our study is to evaluate moral competence and moral attitudes of Czech and foreign general medicine students at the Medical Faculty of Charles University in Hradec Králové, and to find out the dependence of these parameters on several factors (age, school year, nationality, sex, religion and life satisfaction). In this transversal study, 310 Czech and 70 foreign students of the 1st – 5th school years have been tested by means of the Czech and English MJT versions (Moral Judgement Test, Georg Lind).

Moral competence in Czech students is significantly decreasing as they grow older whereas in foreign students it is non-significantly increasing. In Czech students, moral competence is significantly increasing when there is greater life satisfaction. The influence of the other factors

(sex, nationality and religion) on moral competence has not been proven either in Czech, or in foreign students. The level of moral judgement (moral attitude) is post-conventional during their

entire studies (i.e. the 5th and 6th stages according to Kohlberg).

It is gratifying that our students reach the post-conventional level of moral judgement during their entire medical studies. The fact that moral competence is decreasing as they grow older can also be explained in an optimistic way – namely that the younger medical students are morally more competent than the older ones.

Address for correspondence: Birgita Slováčková, Department of Psychiatry, University Hospital, Hradec Králové 500 05, Czech Republic

Title of the research project: The prognostic importance of biochemical monitoring in gerontology

Grant Agency: Ministry of Health

Project Number: NG/1-3

Principal Researcher: RNDr. Dagmar Solichová

Joint Researchers: doc. MUDr. Vladimír Bláha, CSc., prof. MUDr. Zdeněk Zadák, CSc., RNDr. Miluše Brátová, RNDr. Petr Žďánský, CSc., MUDr. Božena Jurašková, MUDr. Bohuslav Melichar

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 2000000

Summary of 2000 results

Title of the presentation: Bioanalysis of lipid metabolism in nonagenarians

Authors: Dagmar Solichová, Božena Jurašková, Vladimír Bláha, Miluše Brátová, Petr Žďánský, Zdeněk Zadák

Department of Metabolic Care and Gerontology, Teaching Hospital, 500 05 Hradec Králové, Czech Republic

The aim of the present study was the bioanalysis of lipid metabolism in the aged patients and to study the relationship between these biochemical markers and longevity.

Eleven nonagenarians, 9 women and 2 men, aged 94 ± 3 years and ten control patients, 6 women and 4 men, aged 84 ± 5 years, followed at the Department of Metabolic Care and Gerontology, Charles University, Teaching Hospital entered the study. At the start of the project the free fatty acids (FFA), thiobarbituric reactive substances (TBARS), retinol, alpha tocopherol, ascorbic acid, cholesterol, triacylglycerols, phospholipids in serum, in lipoprotein fractions and fatty acids (FA) and phospholipids in erythrocyte membrane were determined. We used capillary gas chromatography for determination of fatty acids. Retinol and alpha-tocopherol were analysed by reversed-phase high-performance liquid chromatography, other parameters were determined spectrophotometrically or spectrofluorometrically. We used Mann - Whitney test for statistical analysis, $P = 0,05$ (NCSS 6.0.21. Kaysville, Utah, 1996). We found significantly higher LDL polyunsaturated fatty acids (PUFA) 22:4n-3 ($p = 0,028$) and 22:6n-3 ($p = 0,018$) and a significant increase of HDL alpha tocopherol / cholesterol ratio ($p = 0,034$) in nonagenarians. There were not any significant differences in erythrocyte membrane fatty acids and phospholipids. In serum we found significantly higher level of TBARS ($3,22 \pm 1,22$ vs. $1,98 \pm 0,71$ $\mu\text{mol/l}$, $p = 0,012$) in nonagenarians, other parameters were not changed significantly.

We conclude that higher concentration of PUFAs in LDL and alpha tocopherol in HDL might be parameters concerning longevity.

Project was supported by Ministry of Health Grant Agency, No NG/1-3.

Address for correspondence: Dagmar Solichová, Dept. of Metabolic Care and Gerontology, Teaching Hospital, 500 05 Hradec Králové, Czech Republic

Title of the research project: Possibility of effect of restenosis implantation of radioactive stents with a very low activity, brought about by cyclotron.

Grant Agency: Ministry of Health

Project Number: 4786-3/98

Principal Researcher: : MUDr. Josef Štásek, Ph.D.

Joint Researchers: MUDr. Pavel Červinka, prof. MUDr. Vladimír Pidrman, DrSc, MUDr. Vladimír Rozsival, CSc., prim. MUDr. Ing. Vižďa, prim. MUDr. Petr Tilšer, Ing. Jan Štursa, Ing. Václav Koudelka, Ing. Miroslav Fišer

Starting date: 1.1.1998

Duration (years): 4

Funds allocated for project - total in Czech crowns: 394000

Summary of 2000 results

Title of the presentation: : Possibility of effect of restenosis implantation of radioactive stents with a very low activity, brought about by cyclotron.

Authors: MUDr.P.Červinka(1), prof. MUDr.Vl. Pidrman(1), DrSc, MUDr.Vl.Rozsival, CSc.(2), prim. MUDr. Ing.J.Vižďa(3), prim. MUDr.P.Tilšer(4), Ing.J.Štursa(5), Ing. V.Koudelka(6), Ing.M.Fišer(5)

2nd Dept.of Med.(1), 1st Dept.of Med.(2), Dept. of Nuclear Med.(3), Dept. of Cardioplulm. and Vasc.Diagnosis(4), Cardiosurgery Clinic(6) Faculty Hospital HradecKrálové, Academy of Science, Czech Republic(5)

During year 2 000 we got a licence of the Agency of Nuclear Security of Czech Republic for use of radioactive stents in human.The licence has been valid from 1.9.2 000. We finished the methodology of irradiation of stents in cyclotron till this time. We set activity of our stents into 40 mCi in the time of application.

We have started with application of radioactive stents to patients in the beginning of September . We haven't had any complication due to application of radioactive stents . Only one patient had neutropenia because of the treatment by Ticlopidine. Leucocytes returned to normal level after termination of Ticlopidine. We hope that we will finish the application of radioactive stents during the shortest time. The patients will undergo control angiography and IVUS assesment after completion six-month follow up. After it we will summarize and publish our results .

Address for correspondence: MUDr. Josef Štásek, Ph.D., 2nd Dept. of Medicine, Charles University Medical Faculty, Hradec Králové, Czech Republic

Title of the research project: Second year report: Hardware and software solutions for collecting, storing, and analyzing data

Grant Agency: Ministry of Education

Project Number: 111500004

Principal Researcher: Pravoslav Stránský

Joint Researchers: Miroslav Červinka, Zdeněk Dvořák, Karel Hodík, Miroslav Kuba, Jan Novák, Jindra Šmejkalová, Vlasta Tošnerová

Starting date: 1.1.2000

Duration (years): 5

Funds allocated for project - total in Czech crowns: 1678000

Summary of 2000 results

Title of the presentation: Hardware and software solutions for data collection, their storing and analysis

Authors: Pravoslav Stránský (1), Josef Hanuš (1), Vladimír Mašín (1), Libor Straka (1), Miroslav Červinka (2), Jan Kremláček (3) Jan Novák (4) and Jindra Šmejkalová (5)
Fac. Med., Charles Univ., Hr. Králové: Dept. Biophysics (1), Dept. Biology (2), Dept. Pathophysiology (3), Dept. Ophtalmology (4) Dept. Preventive Medicine (5)

Work in the second year of the project (consistent with the research proposal; see <http://camelot.lfhk.cuni.cz/fyzika/>) concentrated mainly on testing the hardware underpinning databases created during the project's initial year. Major effort was also directed toward upgrading the disc arrays of servers and testing the servers for the Windows 2000 and Linux operating systems. The RAM capacity for processing of data was upgraded, and new CDRW mechanics were purchased for backing-up of data.

Other purchases during the second year were a special-purpose graphic card for generating visual stimuli (as part of the evoked potential analysis program); an interface for transferring data from the ultrasonograph into PC readable data files; and software purchases consisting of five licenses for the STATISTICA 5.5 package plus renewal of the MathLab license.

In the second year, publication was made, in electronic form, of the paper that describes digitization and analysis of pictures, and included data storage. During the second year, the electrophysiology group continued with their development of software for cortex-evoked potentials induced by pattern reversal and motion-onset visual stimuli. The other research team's achievements during this year included their using of databases created in collaboration with clinical departments to analyze the results of phacosurgery; creation of a phacosurgeon learning curve; and the storage and retrieval of clinical data for examining the function and morphology of the thyroid gland in patients with systemic lupus erythematoses, rheumatoid arthritis, and osteoarthritis. The group also made a determination of normal values of body sway and their variability. The values will be used in an expert system for computer-based diagnostic decision making in motional disturbances.

Address for correspondence: Pravoslav Stránský, Dept. of Medical Biophysics, Faculty of Medicine in Hradec Králové, Šimkova 870, 500 01 Hradec Králové 1, Czech Republic

Title of the research project: Enhancement of theoretical and practical preparatory of paedodontic students

Grant Agency: Ministry of Education

Project Number: 1861/2000

Principal Researcher: Lucie Strnadová

Joint Researchers: -

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 75000

Summary of 2000 results

Title of the presentation: Enhancement of theoretical and practical preparatory of paedodontic students

Authors: Lucie Strnadová

Fac. Med., Charles Univ., Hr. Králové: Dept. of Dentistry

The sum of money was used to acquire a new PC set, which enhances the efficiency of tuition and prepares advanced theoretical bases of all students of paedodontics. Furthermore it makes possible to work out a new range of tests with picture documentation by using a selection of slides from the clinical collection. The PC set helps preparing graphical tools for practical exercises (materials, preparation methods, picture presentations etc.) The program for students advancement testing is also partly enrolled, and the PC set enables to store the results of each one student.

Project was supported by the Ministry of Education Grant Agency, No 1861/2000.

Address for correspondence: L. Strnadová, Dept. of Dentistry, Faculty Hospital, Hradec Králové, 500 05, Czech Republic

Title of the research project: Electrophysiology of the visual functions in diabetics

Grant Agency: Ministry of Health

Project Number: 4564-3

Principal Researcher: Jaromír Svěrák

Joint Researchers: Jaroslav Peregrin, Eva Rencová, Hana Langrová, Josef Kvasnička, Hana Dvořáková
Dept. Ophthalmology, Faculty Hospital, Hradec Králové

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 279.000

Summary of 2000 results

Title of the presentation: Electrophysiology of the visual functions in diabetics

Authors: Svěrák J. Rencová E., Peregrin J., Kvasnička J.

Redaction of the amplitudes of various components of the electroretinogram (ERG) has been reported frequently in diabetic retinopathy. Of particular interest are the oscillatory potentials. Practically no attention has been paid, however, to the amplitudes and latencies of the scotopic (rod) responses.

ERG examinations according the international standard (rod and maximal responses and oscillatory potentials as well - in 93 diabetics has been performed) 42 patients with normal fundus picture, 27 persons with simple diabetic retinopathy and 27 patients with pre- and proliferative retinopathy.

Significant reduction of amplitudes and prolonged latencies of the scotopic b-waves in rods potentials has been observed even in patients without any diabetic fundus changes. These abnormalities were related to the retinopathy severity. Similar changes have been observed in the oscillatory potential amplitudes and latencies. Discriminant analysis showed that in patients with a reduction of b-wave amplitude below the value of 150 μ V severe fundus alterations are to be expected.

Address for correspondence: J. Svěrák, Dept. Ophthalmology, Faculty Hospital, Sokolská 1, Czech Republic

Title of the research project: Standardisation of tests on force platform as objective method of movement system

Grant Agency: Ministry of Health

Project Number: 6078-3/2000

Principal Researcher: Vlasta Tosnerova

Joint Researchers: Ivan Krekule, Libor Straka, Eva Vanaskova, Zdenek Milacek

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns:

Summary of 2000 results

Title of the presentation: Standardisation of clinical tests on force platform

Authors: Vlasta Tosnerova (1), Ivan Krekule (2), Libor Straka (3), Vanaskova Eva (4), Milacek Zdenek (5)

Dept. of Rehabil, Teach. Hospit., Hr.Kr.(1), Inst. of Physiol., Acad. of. Sci.,Prague (2), Fac.Med..Hr.Kr.of Charl.Univ., Dpt. of Biofysics (3), Vanaskova Eva, Dpt. of Rehabil., Teach. Hosp., Hr.Kr. (4), Milacek Zdenek (Dpt. of Rehabil., Teach. Hosp., Hr.Kr. (5)

Upright posture in human represents a dynamic equilibrium between various disturbances and contractions of musculature resulting in continuous - body sway. The body sway measurement is usually accomplished by evaluation of the trajectory of the center of pressure (CP) of the vertical foot-ground reaction forces by using a force platform (FP) equipped with strain gauge sensors. The trajectory of the CP is related to the asymmetry of the contact area of the feet with ground, i.e. between the length and the width of both feet. It also corresponds to the form of the "stability" ellipsis on the ground, i.e. a curve inside of which should stay the vertical projection of the centre of gravity. Sway of 50 healthy persons (20 males, 30 females), aged 20-25 years, all students of University in Hradec Kralove were examined. Their overall body status (fitness) was evaluated before the FP investigation (e.g. body symmetry, muscle development, medical history etc). Sway during a 20s time interval was described by the both: i/ 2D trajectory of the CP, and ii/ X-and Y- components of the CP deflection in time, resembling a time series. Pilot results represented by grand average component range in both groups show no significant sometimes or significant differences in different parameters.

Project was supported by Ministry of Health NK6078-3/2000

Literature: Benda, B.J., Riley, P.O., Krebs, D.E.: Biomechanical relationship between center of gravity and center of pressure during standing. IEEE. Trans. Rehab. Eng. 2:1 3-25, 1994

Address for correspondence: V. Tosnerova, Dept. of Rehabilitation, Teaching Hospital, Neervalova 956, Hradec kralove, Czech Republic

Title of the research project: Determination of functional activities and phenotype of tumor infiltrating lymphocytes in patients with ovarian cancer

Grant Agency: Ministry of Health

Project Number: NH/5196-3

Principal Researcher: Miroslava Toušková

Joint Researchers: Jindřich Tošner, Bohuslav Melichar, Jan Krejsek, Otakar Kopecký

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 975000

Summary of 2000 results

Title of the presentation: The phenotype of ascitic fluid lymphocytes in patients with malignancy-related ascites

Authors: Miroslava Toušková, *Jindřich Tošner, **Bohuslav Melichar, Jan Krejsek, Otakar Kopecký

Dept. of Clinical Immunology and Allergy, *Dept. of Gynecology and Obstetrics, **Dept. of Oncology and Radiotherapy, Medical School and Teaching Hospital Hradec Králové

The aim of the present study was to study the phenotype of tumor infiltrating lymphocytes (TIL) in malignancy-related ascites (MRA) of patients with different primary tumors. The phenotype of TIL was examined by two-color flow cytometry in MRA of 50 patients. Interleukin-10 (IL-10) and neopterin (NEO) were determined in ascitic fluid by enzyme-linked immunoassay. MRA in ovarian cancer (OC) had significantly (Mann Whitney test, $p < 0.05$) lower CD3+ (73+12 vs 89 + 5%), CD3+CD8+ (28+9 vs 59 +7%), CD3+CD95+ (30+15 vs 52 + 6 %) and NEO (12.5 + 8.5 vs 22.3 + 6.1 nM), and higher CD3+CD4+ (44+14 vs. 28 + 3 %) cells and CD4/CD8 ratio compared to MRA of malignant melanoma, lower NK cells (12 + 8 vs. 22 + 9 %), and significantly higher CD3+CD45RO+, CD8+CD28+, and CD19+CD86+ compared to MRA of pancreatic cancer, and higher CD19+ (8+4 vs.4 + 3%) and CD19+CD86+ cells compared to gastrointestinal cancer. The presence of hepatic metastases was associated with significantly lower CD3+, CD3+CD4+ and CD3+CD45RO+, and higher CD3+CD25+ and NK cells. CD3+HLA-DR+, CD3+RA+, CD3+CD80+, CD8+CD57+, CD3+CD95+, CD86+ and dendritic cells, and concentrations of IL-10 were similar in patients with different primaries. In OC, IL-10 concentrations showed a significant (Spearman rank coefficient, $p < 0.05$) correlation with NEO ($r_s = -0.57$), CD3+CD80+ ($r_s = -0.493$), CD8+CD28+ ($r_s = 0.481$), and NEO with CD3+CD80+ ($r_s = 0.49$), and CD8+CD28+ ($r_s = -0.519$). In conclusion, most of TIL are CD3+ cells and have memory phenotype, while a minor population of cells expresses activation markers, costimulatory molecules, or naive cell phenotype. Differences were observed in TIL phenotype of patients with different primaries. TIL phenotype is linked to the local concentrations of immune activation markers.

Project was supported by grant of the Ministry of Health of the Czech Republic NH/5196-3.

Address for correspondence: M. Toušková, Department of Clinical Immunology and Allergy, Teaching Hospital, Hradec Králové 50005, Czech Republic, touskova@fnhk.cz

Title of the research project: Teaching of gnathology during preclinical dental instruction

Grant Agency: Ministry of Education

Project Number: 1853/2000

Principal Researcher: Dagmar Vahalová

Joint Researchers: Jiří Bittner, David Urie

Starting date: 1.1.2000

Duration (years): 1

Funds allocated for project - total in Czech crowns: 140000

Summary of 2000 results

Title of the presentation: Teaching of gnathology during preclinical dental instruction

Authors: Dagmar Vahalová, Jiří Bittner, David Urie

Fac. Med., Charles Univ., Hr. Králové: Dept. of Dentistry

Gnathology is a science that deals with the study of occlusion and the mandibular movements related to it. It has been developed principally by a group of scientific-minded dentists who seek perfection in articulation practices in restorative dentistry.

The detailed occlusal surface morphology and description of the functional mandibular movements have been incorporated into the preclinical dental instruction in the winter term of the 1. schoolyear. It makes extensive difficulties for the novices to imagine all the complex motions of the mandible. The purchased movement simulator of the mandibular movements for both horizontal and sagittal plane for overhead projectors Logic I and Logic II represents the great teaching aid to that effect.

During the preclinical dental laboratory instruction the students shape the occlusal surfaces of lateral teeth by means of the wax-added technique utilizing different colors of wax, specialized shaping instruments by P. K. Thomas and casts mounted on the articulator. The students learn in this way the basic structure of the occlusal surface and the relationship between the dental arches during the mandibular movements.

Project was supported by the Ministry of Education Grant Agency, No 1853/2000

Address for correspondence: D.Vahalová, Dept.of Dentistry, Faculty Hospital, Hradec Králové, 500 05, Czech Republic

Title of the research project: The intensive cyclic chemotherapy with support whole blood rich in PBPC in treatment breast cancer.

Grant Agency: IGA MZ ČR

Project Number: 4569-3

Principal Researcher: Jaroslav Vaňásek 1

Joint Researchers: Stanislav Filip 1, Jiřina Vávrová 2, Milan Bláha 4, Doris Vokurková 3
1 Dept of Oncology and Radiotherapy, 2 Military Medical Academy, 3 Dept of Immunology, 4 Dept of Hematology and Oncology Charles University Hospital, Hradec Králové, Czech Republic

Starting date: 1.12.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 300000

Summary of 2000 results

Title of the presentation: The intensive cyclic chemotherapy with support whole blood rich in PBPC in treatment breast cancer.

Authors: Stanislav Filip 1, Jiřina Vávrová 2, Milan Bláha 3, Měříčka Pavel
1 Dept of Oncology and Radiotherapy, 2 Military Medical Academy, 3 Dept of Hematology and Oncology UK, Tissue Bank University Hospital, Hradec Králove

Clinical part:

The efficacy of autologous peripheral stem cells given as mobilized whole blood or leukapheresis product for hematopoietic rescue after intensive chemotherapy was studied in 34 consecutive female patients with high-risk breast cancer. All patients received six cycles of chemotherapy regiment EC /Epirubicin 120 mg/m² and cyclophosphamide 830 mg/ m²/ at 14-days intervals. In the cycles with whole blood support, the mean values of applied progenitors per cycle were CD34+cells 1.52x10⁶/kg, CFU-GM 1.18x10⁵/kg, BFU-E 2.54x10⁵/kg, CFU-GEEM 0.31x10⁵/kg. In the courses with cryopreserved PBPC support /leukapheresis product/, the mean values of progenitors were CD34+cells 2.04x10⁶/kg, CFU-GM 1.59x10⁵/kg, BFU-E 2.87x10⁵/kg, CFU-GEEM 0.34x10⁵/kg. Leukopenia in patients supported with whole blood versus leukapheresed PBPC was as follows: grade 4: 38.2% vs 17.6%, grade 3: 55.9% vs 70.6%, grade 2: 20.6% vs 38.6%, and grade 1: 17.6% vs 17.6%. Thrombocytopenia was- grade 4: 32.4% vs 17.6%, grade 3: 29.4% vs 20.6%, grade 2: 20.6% vs 38.2%, grade 1: 17.6% vs 17.6% respectively.. The median follow up analysis was 24.6 /range 7-36/ months. In 21 patients with measurable disease the response rate was 94%, CR 80%, PR 14.

Experimental part:

MiniMACS isolated AC133+cells contained a mean of 85% (80-90) AC133+ cells and coexpressed 80% CD34+, 6.6% CD33+, and 2% CD15+ cells. Flow-cytometric analysis indicated that AC 133+cells were isolated from cells population with low granularity (SS). After a seven days ex vivo expansion in the presence of SCF + IL-3 +IL 11, the number of cells increased 19.4 times. The mean value of CFU-GM in the culture increased 45-fold, BFU-E 5- fold. After 7 days expansion with SCF + IL-3 +IL 11 cells expressed a mean of 12% CD 34+, 8% AC 133+, 59% CD33+ and 30% CD15+.

Address for correspondence: MUDr. Stanislav Filip, Oncology and Radiotherapy dept. Charles university, University Hospital Hradec Králové

Title of the research project: Antioxidative defence system in dyslipidemic patients

Grant Agency: Ministry of Health IGA MZ ČR **Project Number:** NB/4540-3

Principal Researcher: Ing. Jaroslava Vávrová

Joint Researchers: Doc. MUDr. Vladimír Palička, CSc., RNDr. Bedřich Friedecký, MUDr. Jana Zajíčková, Mgr. Martin Beránek, PhD, PharmDr. Lenka Plíšková

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 205000

Summary of 2000 results

Title of the presentation: Antioxidative defence system in dyslipidemic patients

Authors: J. Vávrová, V. Palička, B. Friedecký, J. Zajíčková, M. Beránek, L. Plíšková

Institute of Clinical Biochemistry and Diagnostics, Faculty Hospital, Charles University, Hradec Králové, Czech Republic

The key role of antioxidants has been identified as a preventive factor for atherosclerosis. Making use of the available instrumentation a new analytical method of vitamin C determination in biological materials was developed and optimised. This method respects knowledge of pre-analytical phase: sampling, preparation and storing of biological material. Determination of ascorbic acid and its metabolite dehydroascorbic acid was carried out by high performance capillary electrophoresis (CE). Analytical conditions of pre- and post-analytical phases was in the focus of our interest as well as parameters evaluation in the lipoprotein fractions after ultracentrifugation. Examined analytes: vitamin A, vitamin E, products of lipid peroxidation, cholesterol, triglycerides. We determined serum vitamins (A, E, C), serum lipid concentration (cholesterol + triglycerides), serum lipid peroxidations parameters and lipoprotein fractions vitamins A, E and lipid concentration in the group of 60 dyslipidemic patients. Our results show good correlation between vitamin E and lipid concentration (cholesterol + triglycerides) in VLDL ($r = 0,93$) and LDL ($r = 0,92$) fractions. The positive effect of vitamin E supplementation in dyslipidemic patients is apparent. In sixty hyperlipidemic patients was observed a possible effect of apolipoprotein E genotype as an independent risk factor of atherosclerosis on efficiency of hypolipidemic therapy. Genotypes of apo E were determined by PCR/RFLP method. The final project phase was dealt with antioxidation system in "in vitro" experiment. The goal was to determine the influence of particular lipoprotein sub fractions to endothelial cells in the presence of oxidative stress after its initialisation.

Address for correspondence: J.Vávrová, e-mail: VavrovaJ@LFHK.cuni.cz

Title of the research project: Contribution of Colour Duplex Ultrasound to the Diagnostics of Peripheral Occlusive Arterial Disease.

Grant Agency: Ministry of Health

Project Number: NA/4560-3

Principal Researcher: Petr Vodnansky

Joint Researchers: Pavel Elias, Miroslav Lojik, Antonin Krajina, Jan Fridrich

Starting date: 1.1.1998

Duration (years): 3

Funds allocated for project - total in Czech crowns: 600000

Summary of 2000 results

Title of the presentation: Contribution of Colour Duplex Ultrasound to the Diagnostics of Peripheral Occlusive Arterial Disease.

Authors: Petr Vodnansky 1), Pavel Elias 2), Miroslav Lojik 2), Antonin Krajina 2), Jan Fridrich 1)

1) Dept. of Cardiopulmonary and Vascular Diagnostics, 2) Dept. of Radiology
Faculty Hospital, Hradec Kralove, Czech Republic

Aim. In patients with peripheral occlusive arterial disease (PAOD) severity, localisation and length of arterial affection influence principally the method of treatment. In this study the authors determined the accuracy of information about the peripheral arteries obliteration's character gained by colour duplex ultrasound (CDU). Angiography (AG) was chosen as a comparative method.

Material and method. Patients with claudications and critical limb ischaemia were included in the study. Arterial system was visualised from subrenal aorta to the level of ankle. The stenosis was quantified by peak systolic velocity ratio. Absence of the signal in colour as well as spectral Doppler record is the main diagnostic criterion of obliteration. Obliterations in the femoropopliteal segments were divided into short ones (shorter than 10 cm) and long ones (longer than 10 cm).

Results. 174 patients (220 lower extremities and 1413 arterial segments) were examined ultrasonographically and compared with angiography. 389 pathological affections were found. Total accuracy of CDU for prediction of stenosis greater than 50% and obliteration was 95%, sensitivity was 90% and specificity was 97%.

Conclusion. CDU is an accurate non-invasive method for determination of haemodynamically significant affections of arterial system in aortoiliac, femoropopliteal as well as crural area. CDU shows high accuracy in determination of localisation, character and length of occlusion or stenosis. High agreement between CDU and AG enables to choose patients suitable for PTA only on the basis of CDU results

Address for correspondence: Petr Vodnansky, M.D. OKVD, Faculty Hospital, Hradec Kralove, P.C. 500 05, Czech Rep., email: vodnanskyp@lfhk.cuni.cz

Title of the research project: Analysis of expired gases using GC/MS for observation of metabolic disorders - a cooperative project of three faculties

Grant Agency: Czech Republic

Project Number: 203/99/1165

Principal Researcher: Gasparič Jiří, prof. ing., DrSc.

Joint Researchers: Zadák Zdeněk, prof. MUDr., CSc.

Starting date: 1.1.1999

Duration (years): 3

Funds allocated for project - total in Czech crowns: 213000

Summary of 2000 results

Title of the presentation:

Authors:

This research project is solved by three faculties. The Department of metabolic care and gerontology is working on analytical and clinical part of the project. During the second year pilot studies on breath isoprene excretion were performed to find out possible applications of this non-invasive test (intensive care units, LDL apheresis ect.). Also, this test was used to evaluate the cholesterol synthesis rate in the patients suffering from rare metabolic disorders.

The results were published as follows:

Internal Medicine: The role of cholesterol and its precursors in the intensive care and parenteral nutrition

11th International Symposium on Pharmaceutical and Biomedical Analysis: Complex determination of cholesterol precursors in various human matrices by GC/MS

Advances in Chromatography and Electrophoresis: Preanalytical phase in the determination of cholesterol precursors in human matrices

The origin of isoprene from mevalonate was successfully demonstrated on the basis of acid catalysis and precise mechanism was found.

The method for determination of methane in expired air was developed and will be used for monitoring of fiber influence on colonic microflora.

Address for correspondence: Department of metabolic care and gerontology, Teaching Hospital, Hradec Králové 500 05, Czech Republic

Title of the research project: Changes of lipid metabolism and its mediator-related effects in patients with colorectal carcinoma - prospective impact in nutritional support

Grant Agency: Ministry of Health

Project Number: NC/6171-3

Principal Researcher: Zadák Zdeněk, prof. MUDr. CSc.

Joint Researchers: RNDr. Petr Žďánský, MUDr. Bohuslav Melichar, MUDr. Pavel Jandík, RNDr. Dagmar Solichová, doc. MUDr. Vladimír Bláha, CSc.

Starting date: 1.1.2000

Duration (years): 3

Funds allocated for project - total in Czech crowns: 385000

Summary of 2000 results

Title of the presentation: see above

Authors: see above

During the first year of this project available reference data were collected. Necessary analytical methods were developed - the determination of squalene, lathosterol and lanosterol in plasma and the determination of mevalonic acid in urine. The latter method is not available in the Czech Republic and its large application in the project is supposed.

Also, the sampling protocol was developed and the clinical part of research will begin in January.

Some methodologies or results of pilot studies were accepted for publication or already published (examples):

European Journal of Cancer 36: 1844-1852 (2000): TNF modulates differentiation induced by butyrate in the HT-29 human colon adenocarcinoma cell line

Journal of Pharmaceutical and Biomedical Analysis (in press): Bioanalysis of age-related changes of lipid metabolism in nonagenarians

Internal medicine (11/2000) The role of cholesterol and its precursors in intensive care and parenteral nutrition

During the second year of research project the data from colorectal adenocarcinoma patients and control subjects will be collected. Also, some additional biochemical methods will be developed for the evaluation of the metabolism of polyunsaturated fatty acids.

Address for correspondence: Department of metabolic care and gerontology, Teaching Hospital, Hradec Králové 500 05, Czech Republic