

--如何作研究--

新光醫院急診科主任
王宗倫 醫師

為什麼要作研究？

- 學術地位？
- 研究獎金？
- 升等需求？
- 消遣娛樂？
- 為往聖繼絕學，為萬世開太平！！

研究的種類

- ✿ 心血來潮的研究
- ✿ 東坡肉型的研究
- ✿ 斷頭型的研究
- ✿ 老鼠會型的研究
- ✿ 不可思議的研究

不可思議的研究

- ✿ **Unskilled and Unaware of It:
How Difficulties in Recognizing
One's Own Incompetence Lead
to Inflated Self-Assessments. /
*Personality and Social
Psychology 1999;77:1121-34***

不可思議的研究

- ★ **On the Comparative Palatability of Some Dry-Season Tadpoles from Costa Rica. *Am Midland Naturalist* 1971;86:101-9**

不可思議的研究

- ★ **Andre Geim and Sir Michael Berry: using Magnets to Levitate a Frog and a Sumo Wrestler
Of Flying Frogs and Levitrons. *Eur J Physics* 1997;18:307-13**

不可思議的研究

- ✦ **Romantic Love may be Indistinguishable from Having Severe Obsessive-Compulsive Disorder.**

Alteration of the Platelet Serotonin Transporter in Romantic Love.
Psychological Medicine
1999;29:741-5

不可思議的研究

- ✦ **Reverend Sun Myung Moon: Bringing Efficiency and Steady Growth to the Mass-Marriage Industry**

不可思議的研究

- ★ **PawSense: a Software that Detects When a Cat is Walking Across Your Computer Keyboard**

不可思議的研究

- ★ **The Collapse of Toilets in Glasgow. *Scottish Medical Journal* 1993;38:185**

不可思議的研究

- ✦ **Magnetic Resonance Imaging of Male and Female Genitals During Coitus and Female Sexual Arousal. *British Medical Journal* 1999;319:1596-1600**

不可思議的研究

- ✦ 結論是 . . .
- ✦ 天下無難事，只怕有心人
- ✦ 只要你肯幹，有什麼不可以

醫學研究的種類

- ✦ 基礎醫學研究
- ✦ 公衛統計研究
- ✦ 臨床醫學研究
 - ✦ 病例報告
 - ✦ 原始論著

由證據醫學想起

- ✦ **Positive RCTs:** A prospective RCT with positive conclusions
- ✦ **Neutral RCTs:** Nonrandomized, prospective observational study of a group that uses new treatment; must have a control group of comparisons
- ✦ **Prospective, nonrandom:** Nonrandomized, **prospective** observational study of a group that uses new treatment; must have a control group for comparisons
- ✦ **Retrospective, nonrandom:** Nonrandomized, **retrospective** observational study; 1 group used new treatment; must have a control group for comparisons

由證據醫學想起

- **Case series: Series of patients received new treatment in past or will receive in future; watch to see what outcomes occur; no control group**
- **Animal studies (A and B): Studies using animals or mechanical models; A-level animal studies are higher quality than B-level studies**
- **Extrapolations: Reasonable extrapolations from existing data or data gathered for other purposes; quasi-experimental designs**
- **Rational conjecture, common sense: Fits with common sense; has face validity; applies to many non-evidence-based guidelines that “made sense”. No sense of harm.**

如何進行研究

- 搜集資料
- 確立目標
- 擬訂計畫
- 建立步驟
- 事前評估
- 開始執行
- 整理資料及分析
- 撰寫論文

搜集資料

- ✦ 依樣畫葫蘆
- ✦ 打蛇隨棍上
- ✦ 五鬼搬運法
- ✦ 去蕪存精，歸納整理

確立目標

- ✦ 與搜集資料相輔相成
- ✦ 目標包括
 - 研究類別
 - 論文定位
 - 其他

擬訂計畫

- ✿ 三個臭皮匠，勝過一個諸葛亮
- ✿ 量力而為，切勿寅吃卯糧
- ✿ 留得青山在，不怕沒柴燒

建立步驟及事前評估

- ✿ 因果關係
- ✿ 充分利用資源
- ✿ 群策群力
- ✿ 評估可行性及預訂進度

開始執行

- ✿ 分工合作：蟲蟲危機
- ✿ 監督制度：共同基金
- ✿ 溝通討論：井底之蛙
- ✿ 整合型計劃的特殊性

整理資料及分析

- ✿ 計劃主持人的角色
- ✿ 整理與執行並行不悖
- ✿ 迴饋機制的必要
- ✿ 統計分析的重要性

撰寫論文

- ✿ 媳婦熬成婆：勿得意忘形
- ✿ 強龍不壓地頭蛇：遵守規定
- ✿ 三分姿色，七分顏色
- ✿ 外來的和尚會唸“洋”經
- ✿ 撞球原則：快、狠、準
- ✿ 鐵杆磨成繡花針

如何撰寫論文

- ✿ **Robert A. Day: How to Write and Publish a Scientific Paper**
 - How to Prepare the Title?
 - How to List the Authors?
 - How to List the Address?
 - How to Prepare the Abstract?
 - How to Write the Introduction?
 - How to Write the Materials and Methods Section?
 - How to Write the Discussion?
 - How to State the Acknowledgements?
 - How to Cite the Literature?
 - How to Design Effective Tables?
 - How to Prepare Effective Illustrations?
 - How to Type Manuscript?
 - **THE REVIEW PROCESS ...**

不是玩笑 . . .

- **The lab test indicated abnormal liver function.**
- **The baby was delivered, the cord clamped and cut, and handed to the pediatrician, who breathed and cried immediately.**
- **Exam of genitalia reveals that he is circus sized.**
- **The skin was moist and dry.**
- **Rectal exam revealed a normal size thyroid.**

不是玩笑 . . .

- **The patient had waffles for breakfast and anorexia for lunch.**
- **She stated that she had been constipated for most of her life until 1989 when she got a divorce.**
- **Between you and me, we ought to be able to get this lady pregnant.**
- **The patient was in his usual state of good health until his airplane ran out of gas and crashed.**

不是玩笑 . . .

- **I saw your patient today, who is still under our car for physical therapy.**
- **The patient lives at home with his mother, father, and pet turtle, who is presently enrolled in day care three times a week.**
- **Bleeding started in the rectal area and continued all the way to Los Angeles.**
- **She is numb from her toes down.**

不是玩笑 . . .

- **Exam of genitalia was completely negative except for the right foot.**
- **While in the emergency room, she was examined, X-rated and sent home.**
- **The patient was to have a bowel resection. However, he took a job as a stockbroker instead.**
- **The patient suffers from occasional, constant, infrequent headaches.**

不是玩笑 . . .

- ✦ **Coming from Detroit, this man has no children.**
- ✦ **Patient was alert and unresponsive.**
- ✦ **When she fainted, her eyes rolled around the room.**
- ✦ **... ..**
- ✦ **不是不會發生在你我身邊**

少縮寫 . . .

- ✦ **NSD:**
 - **Normal Spontaneous Delivery**
 - **Nasal Septal Deviation**
 - **No Sexual Dysfunction**
- ✦ **NKFDA**
 - **No Known Food and Drug Allergy**
- ✦ **EMMPRIN**
 - **Extracellular Matrix Metalloprotease Inducer**
- ✦ **XQ4ME**

接下來是 . . .

睡覺時間 z z z

Ongoing Protocols

- **Basic Research: Effects of Hypoxia on Cardiomyocyte Connexin 43 Expression**
- **Clinical Research:**
 - **Effects of Morphine on Neutral Endopeptidase 24.11 in Heart Failure**
 - **Doppler Patterns in Wide-QRS Tachycardia**
 - **Electromagnetic Effects of Xylophone on AED**
- **Disaster Research: Disaster Response Hospital and Personnel Registration (Dr.Hope Registration)**

Neutral Endopeptidase

24.11

- **Membrane-bound zinc metalloprotease**
- **Hydrolysis of endogenous peptides**
 - **Atrial natriuretic peptide**
 - **Bradykinin**
 - **Substance P**
 - **Endothelins**
 - **Met-enkephalin**
- **Wide distribution: Endothelium, Leukocytes, Epithelium etc.**

Neutral Endopeptidase

24.11

- **Regulation: under investigation**
 - **Leukocyte and Epithelium: decrease by phorbol ester**
 - **Transfected epithelium and Leukemia cells: increase in cell growth and after glucosteroids**
 - **Vascular smooth muscle cells: increase NEP gene transcription and activity by steroids**
 - **ALL cells: casein kinase II**

Neutral Endopeptidase 24.11

★ **Glucocorticoid induce neutral endopeptidase in transformed human tracheal epithelial cells**

Borson DB.
Am J Physiol 1991

Neutral Endopeptidase 24.11

★ **CD10(CALLA)/NEP modulates inflammatory peptide-induced changes in neutrophil morphology, migration, and adhesion proteins and is itself regulated by neutrophil activation**

Shipp MA. Blood 1991

Role of Morphine

★ Clinical Use in Patients with ACS:

- Pain Relief
- Attenuation of Sympathetic Activity
- Morphine Preconditioning
 - Glibenclamide sensitive
 - Glibenclamide insensitive
 - Free Radicals / Mitochondrial ATP-sens. K Channel
- Other Cardioprotective Mechanism?
 - ?NEP

Role of Morphine

★ NEP Activation

- Reduce circulating L-selectin and ICAM-1 in patients with MI
- Other evidences
- Mechanisms: ?
 - Mu-opioid receptors linked to K channels via G proteins
 - Protein kinase A
 - Protein kinase C
 - Tyrosine kinase

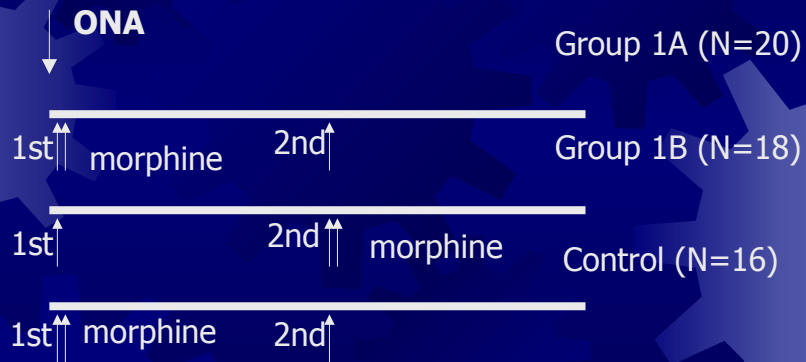
Morphine on NEP

- ★ **Hypothesis: Morphine acts on endothelium and WBC to activate their membrane bound Neutral Endopeptidase 24.11 (NEP) and then degrades vasoactive peptides such as Endothelin-1 (ET-1)**

Past Study-1

- ★ **To investigate the effects of morphine on neutrophil and endothelial activation**
- ★ **Subjects: 38 patients with AMI**
- ★ **Blood sampling: for measurements of**
 - **ICAM-1**
 - **L-selectin**
 - **NEP**

Past Study-1



Past Study-1

- ★ **Neutrophil preparation: heparinized; gradient centrifugation**
- ★ **Measurement of ICAM-1 and L-selectin: commercial ELISA kits**
- ★ **Enzymatic Assays of NEP: Fluorimetric assay (425 nm) using glutaryl-ala-ala-phe-4-methoxy-2-nathylamine as substrate**

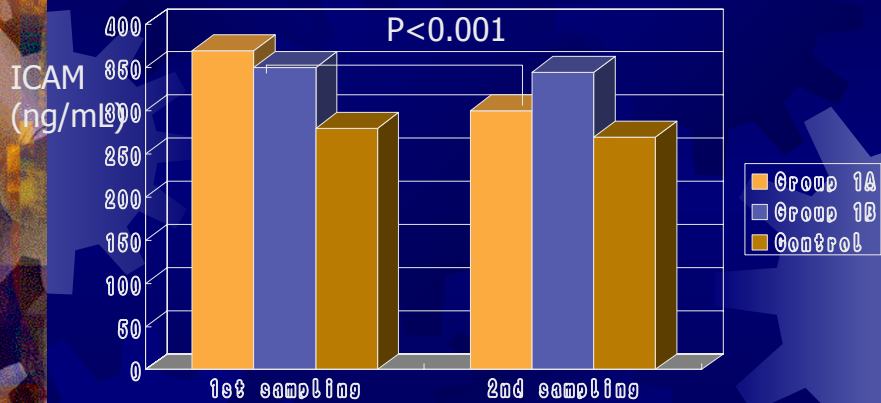
Past Study-1

	Group 1A	Group 1B	Control
Age (yr)	62 _± 15	64 _± 16	60 _± 17
Male (%)	14(70%)	13(73%)	10(63%)
HTN	12	9	9
DM	3	3	2
Smoking	9	8	7
Hyperlipid.	3	4	3

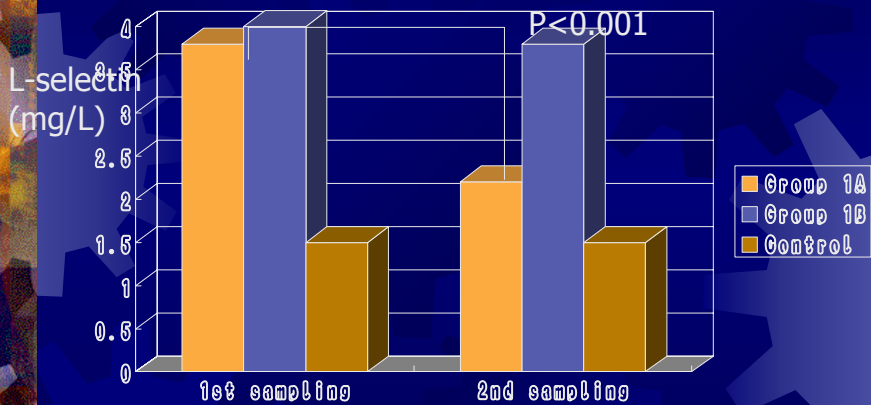
Past Study-1

	Group 1A	Group 1B	Control
Hb (g/dL)	13.5 _± 1.4	13.3 _± 1.4	13.6 _± 1.7
WBC (10 ³)	10.8 _± 3.0	10.0 _± 2.3	6.8 _± 1.0
Neutro. (%)	67 _± 9	68 _± 10	65 _± 10
Mono. (%)	7.6 _± 2.8	7.2 _± 2.6	7.9 _± 3.0
Plat. (10 ³)	286 _± 94	249 _± 86	263 _± 78

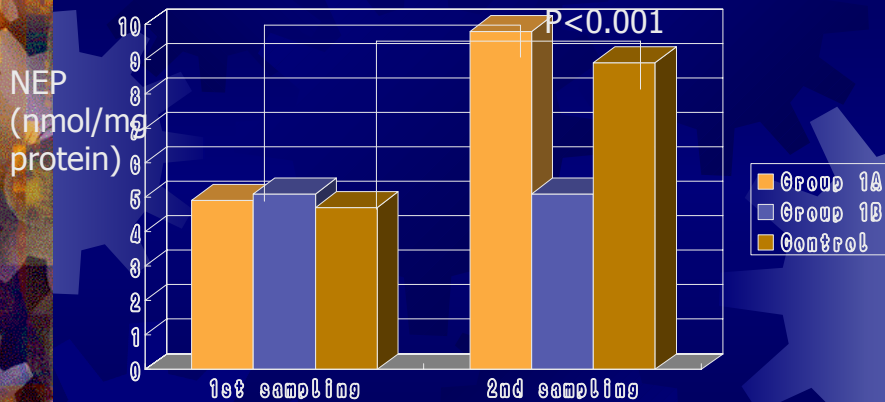
Past Study-1



Past Study-1



Past Study-1



Morphine on NEP

★ CHF

- Group 1: oxygen, NTG, furosemide and blood sampling 1 → morphine → 10 min → blood sampling 2
- Group 2: oxygen, NTG, furosemide and blood sampling 1 → 10min → blood sampling → morphine

★ Control

- Treat as Group 1 and Group 2

Morphine on NEP

- ★ **Leukocyte Separation: Gradient Centrifugation**
- ★ **NEP quantification: DAGNPG as substrate and estimation by spectrofluorometry (342 nm vs. 562 nm)**
- ★ **ET-1 quantification: double antibody sandwich ELISA method**

Doppler on WQT

- ★ **Hypothesis: Doppler flow pattern of pulmonary vein can demonstrate A-V dissociation of ventricular tachycardia among those with wide-QRS tachycardia**

Doppler on WQT

★ Favor VT:

- AV dissociation
- Fusion beat
- Capture beat
- Absence of RS in any precordial leads
- Onset of R to Nadir of S longer than 100 msec
- Morphologic Criteria

Doppler on WQT

★ Favor VT: (RBBB morphology)

- V1-2: monophasic or biphasic
- V6: Q wave, R-to-S ratio < 1, QS, QR or monophasic R

★ Favor VT: (LBBB morphology)

- V1-2: R duration > 30 msec; duration from onset of R to nadir of S > 60 msec; notching in downsloping of S
- V6: QR or QS

Xylophone on AED

- ✦ **Hypothesis: Electromagnetic effects of xylophone may interfere the readings of monitors on AED and thus result in inadequate management**

特別事項

- ✦ 人道精神
- ✦ 鼠道精神
- ✦ 勿落人口實



謝謝

請多指教！！