

# --如何作研究--

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## 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

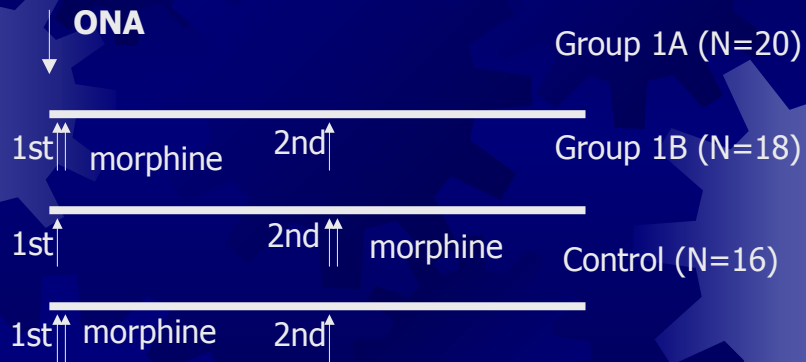
## Morphine on NEP

- ★ **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

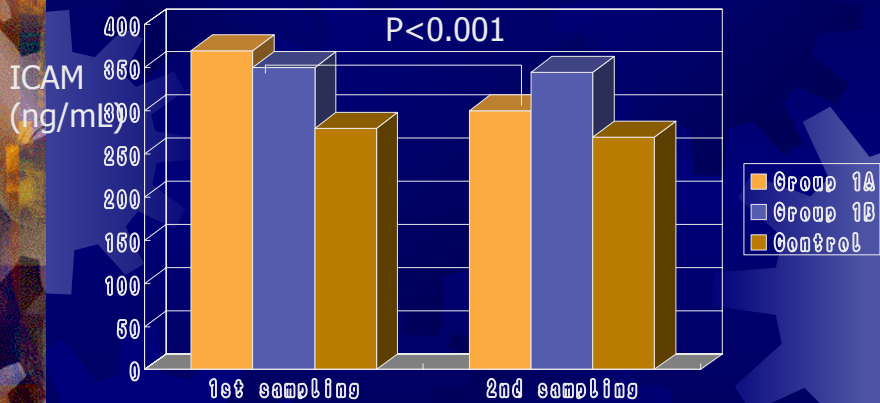
	Group 1A	Group 1B	Control
Age (yr)	62 <sub>±</sub> 15	64 <sub>±</sub> 16	60 <sub>±</sub> 17
Male (%)	14(70%)	13(73%)	10(63%)
HTN	12	9	9
DM	3	3	2
Smoking	9	8	7
Hyperlipid.	3	4	3

## Past Study-1

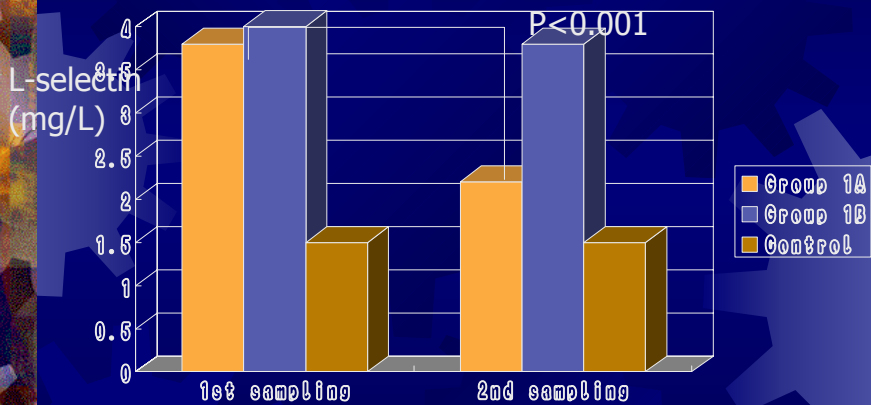
	Group 1A	Group 1B	Control
Hb (g/dL)	13.5 <sub>±</sub> 1.4	13.3 <sub>±</sub> 1.4	13.6 <sub>±</sub> 1.7
WBC (10 <sup>3</sup> )	10.8 <sub>±</sub> 3.0	10.0 <sub>±</sub> 2.3	6.8 <sub>±</sub> 1.0
Neutro. (%)	67 <sub>±</sub> 9	68 <sub>±</sub> 10	65 <sub>±</sub> 10
Mono. (%)	7.6 <sub>±</sub> 2.8	7.2 <sub>±</sub>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



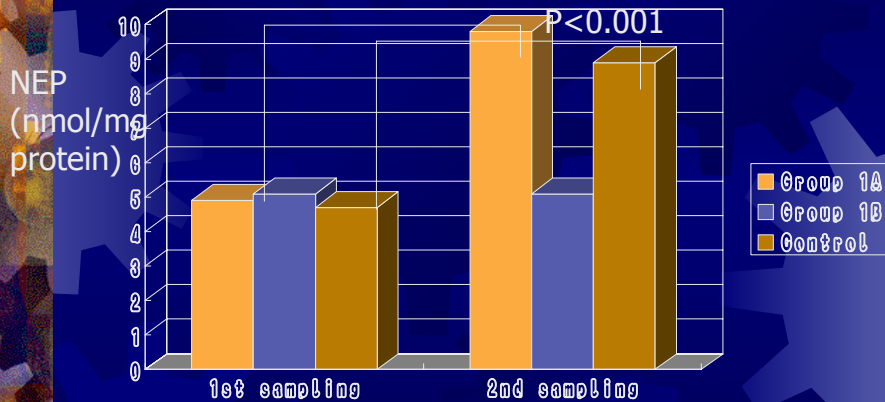
# Past Study-1



# 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！！