

EBM Presentation

Presented by R周炳全

Clinical Scenario

- A 69 year-old male is diagnosed of type 2 DM at 北門衛生所. OAD was prescribed without regular control. This time he was found conscious drowsiness and he was brought to our ER. At ER blood sugar was 49 mg/dL and 50% G/W was given. After glucose supplement, his condition was improved. Then, he was admitted to endocrine ward due to hypoglycemia.

Clinical Scenario

- According to his statement, he hasn't take OAD at least for 2 weeks and he also had diet regularly. After admission, finger sugar was around 80 mg/dl in the morning and around 90~120 mg/dl after meal. HbA_{1C}=5.1%. To assess the possibility of insulinoma, we suggest to arrange 72hr fasting test.

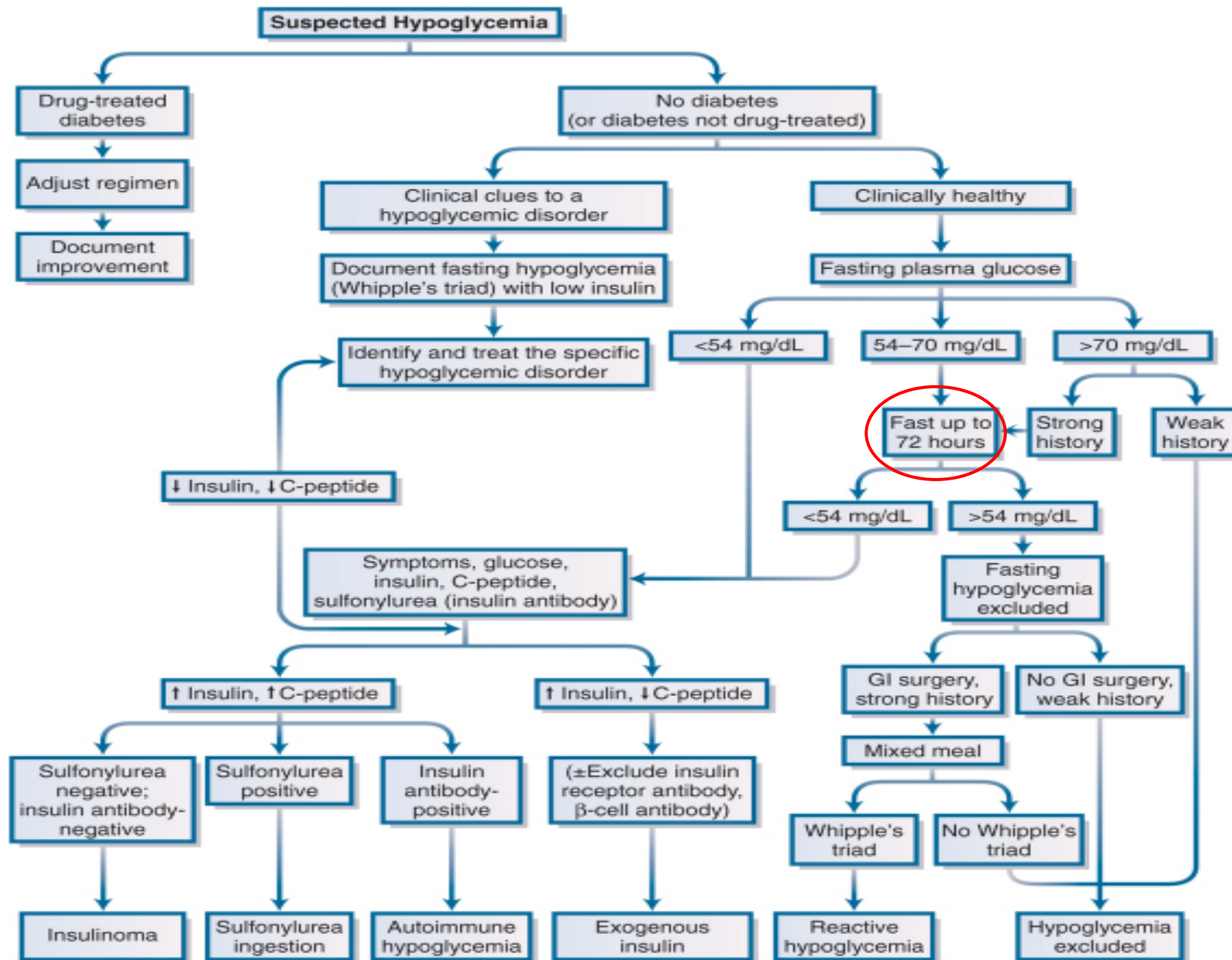


Figure 33-14 Diagnostic algorithm for suspected hypoglycemia. GI, gastrointestinal.

Clinical Scenario

- His son concerns about his father might not tolerance to prolong fasting and he asks if the 72hr fasting test could be shortened.

P	69 year-old male is diagnosed of type 2 DM and suffered from hypoglycemia
I	24~48 hrs of fasting test
C	72 hrs of fasting test
O	Diagnostic rate of insulinoma

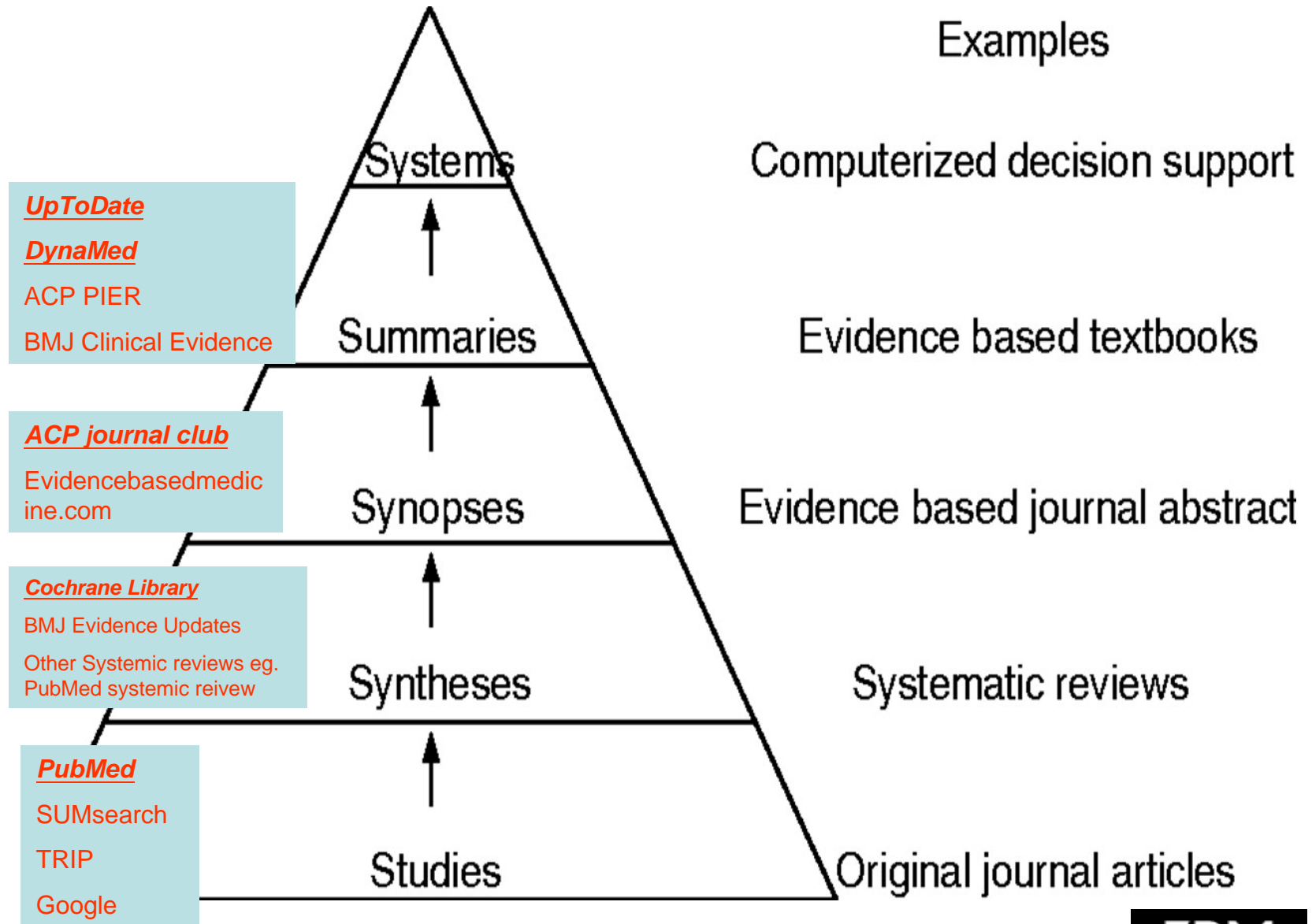
搜尋最有用的資料

先從已經過評讀的database開始找起
(system,summary,synopses,synthesis)

最後再找尚未經過嚴格評讀的study

The "5S" levels of organisation of evidence from healthcare research

Brian Haynes, R Evid Based Med 2006;11:162-164





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- Localization of pancreatic endocrine tumors (islet-cell tumors)
- Noninsulinoma pancreatogenous hypoglycemia

▼ **Topic Outline**

INTRODUCTION

NORMAL RESPONSE TO
HYPOGLYCEMIA

APPROACH TO TESTING

72-HOUR FAST

- Protocol
 - Test end points and duration
 - Ending the fast



- Fasting for a maximum of 72 hours has been the standard test for the diagnosis of insulinoma.
- A 48-hour maximum has been proposed as a simpler alternative based upon a report of **127 patients** with insulinoma in which adequate information was obtained for diagnosis in all patients . The fast was terminated because of hypoglycemia (plasma glucose ≤ 45 mg/dL [2.5 mmol/L]) in 43 percent by 12 hours, 67 percent by 24 hours, and **95 percent by 48 hours**.
- However, in our series of 205 patients with insulinoma, **14 percent** did not develop Whipple's triad until **after 48** hours of fasting . Thus, to avoid misdiagnosis, we recommend the standard 72-hour fast.

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- No relative information about prolong fast test except of standard 72 hours fast test was found.

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Forty-Eight-Hour Fast: The Diagnostic Test for Insulinoma

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H. R. ALEXANDER, J. L. DOPPMAN, M. C. SKARULIS, AND P. GORDEN

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The Journal of Clinical Endocrinology & Metabolism
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- Data obtained during the supervised fast of patients with **pathologically** proven insulinoma over a 30-yr period (1970 –2000) were reviewed
- Mean age: 42.7 ± 15.9 yrs(13-81 y/o)
total 127 patient
- The fast was terminated due to hypoglycemia in 44 patients (42.5%) by 12 h, 85 patients (66.9%) by 24 h, and **120 (94.5%) by 48 h.**

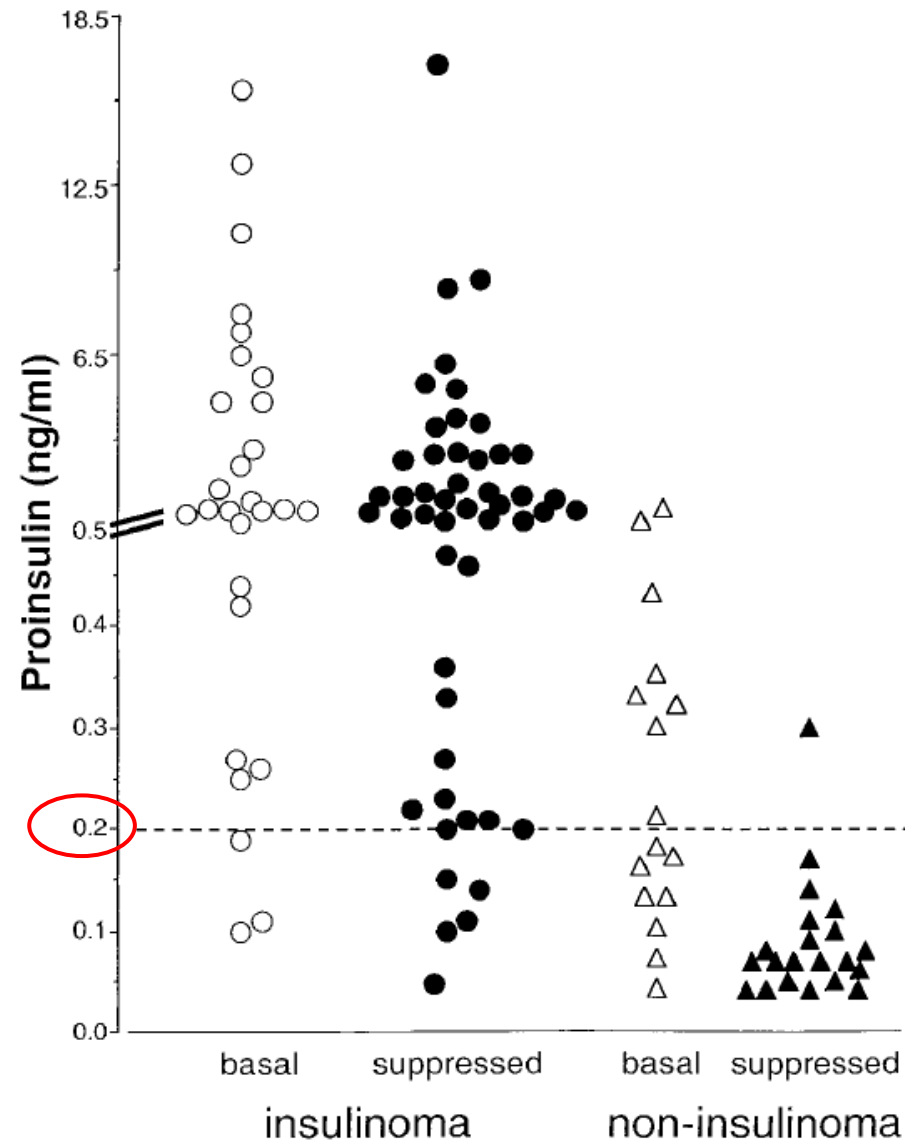


FIG. 2. Direct immunoreactive proinsulin measurements in patients with and without insulinoma. Basal refers to the beginning of the fast, and suppressed refers to the end of the fast. Note that samples were available in 42 insulinoma patients (basal) and 50 suppressed patients. Twenty-eight of these samples have been previously reported and correlated with measurements of plasma proinsulin-like component (10). In the noninsulinoma patients, there were 16 samples obtained in the basal state, and 21 in the suppressed state.

CLINICAL PERSPECTIVE

The Prolonged Fast

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- The Mayo Clinic experience of positive fasts within 48 h in large series of patients with insulinoma has been reported as: **94%** (n =108, 1927–1965) and **92%** (n = 51, 1964–1975).
- In the subsequent period, 1976 to the present, we have **histological confirmation** in 205 patients operated on for insulinoma. Among these, **170 underwent prolonged fasts** according to a standard protocol.
- The fast was terminated within 12 h in 33%, 24 h in 65%, 36 h in 84%, **48 h in 93%**, and 72 h in 99%. Two patients had negative fasts at 72 h; in one the fast remained negative through 96 h.

- For instance, in recent years we have subjected **noninsulinoma hypoglycemic patients** to the prolonged fast who subsequently had the following diagnoses: insulin factitious hypoglycemia, sulfonylurea factitious hypoglycemia, end-stage renal disease, nonislet cell tumor hypoglycemia, insulin autoimmune hypoglycemia, drug-induced hypoglycemia, and noninsulinoma pancreatogenous hypoglycemia syndrome. **In 14% of these patients with positive fasts,** Whipple's triad developed after 48 h of fasting.

□ **1:** [Horm Metab Res.](#) 2007 Jul;39(7):507-10.

Assessment of suspected insulinoma by 48-hour fasting test: a retrospective monocentric study of 23 cases.

[Quinkler M](#), [StreLOW F](#), [Pirlich M](#), [Rohde W](#), [Biering H](#), [Lochs H](#), [Gerl H](#), [Strasburger CJ](#), [Ventz M](#).

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- In a retrospective study, we identified 39 patients (24 females, 15 men; average age 47 years [range 12-78 years]) with insulinoma.
- The fast was terminated due to neuroglycopenic symptoms in 4 patients (17.4%) at the 12th hour, in 17 patients (73.9%) at the 24th hour, and in 22 patients (95.7%) at the 48th hour.

Level of evidence

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

Level	Therapy/Prevention, Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	SR (with <u>homogeneity*</u>) of RCTs	SR (with <u>homogeneity*</u>) of inception cohort studies; <u>CDR†</u> validated in different populations	SR (with <u>homogeneity*</u>) of Level 1 diagnostic studies; <u>CDR†</u> with 1b studies from different clinical centres	SR (with <u>homogeneity*</u>) of prospective cohort studies	SR (with <u>homogeneity*</u>) of Level 1 economic studies
1b	Individual RCT (with narrow <u>Confidence Interval‡</u>)	Individual inception cohort study with <u>≥ 80% follow-up</u> ; <u>CDR†</u> validated in a single population	Validating** cohort study with <u>good‡‡‡</u> reference standards; or <u>CDR†</u> tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	<u>All or none§</u>	All or none case-series	Absolute SpPins and SnNouts‡‡	All or none case-series	Absolute better-value or worse-value analyses ‡‡‡
2a	SR (with <u>homogeneity*</u>) of cohort studies	SR (with <u>homogeneity*</u>) of either retrospective cohort studies or untreated control groups in RCTs	SR (with <u>homogeneity*</u>) of Level >2 diagnostic studies	SR (with <u>homogeneity*</u>) of 2b and better studies	SR (with <u>homogeneity*</u>) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of <u>CDR†</u> or validated on split-sample§§§ only	Exploratory** cohort study with <u>good‡‡‡</u> reference standards; <u>CDR†</u> after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with <u>homogeneity*</u>) of case-control studies		SR (with <u>homogeneity*</u>) of 3b and better studies	SR (with <u>homogeneity*</u>) of 3b and better studies	SR (with <u>homogeneity*</u>) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and <u>poor quality cohort and case-control studies§§</u>)	Case-series (and <u>poor quality prognostic cohort studies***</u>)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

P

	Article 1
所取樣本是否有臨床代表性	yes
樣本特性是否與我的病人差不多	yes

總結與討論

- We conclude that with the current available insulin and proinsulin assays, the diagnosis of insulinoma can be made within 48 hr. (sensitivity 93%-95.7%)

CLINICAL STUDY

Insulin, C-peptide and proinsulin for the biochemical diagnosis of hypoglycaemia related to endogenous hyperinsulinism

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- **Objective:** We evaluated the respective value of insulin, C-peptide and proinsulin levels in 33 patients with endogenous hyperinsulinism and in 67 controls to determine the best parameters and thresholds to make or to rule out the diagnosis of endogenous hyperinsulinism.
- **Conclusion:** Proinsulin levels above 5 pmol/l with blood glucose levels below 2.5 mmol/l during a 72 h fast test represent the best criterion for the diagnosis of endogenous hyperinsulinism, reaching **100% diagnostic specificity and sensitivity**.

Thank You for Your Attention