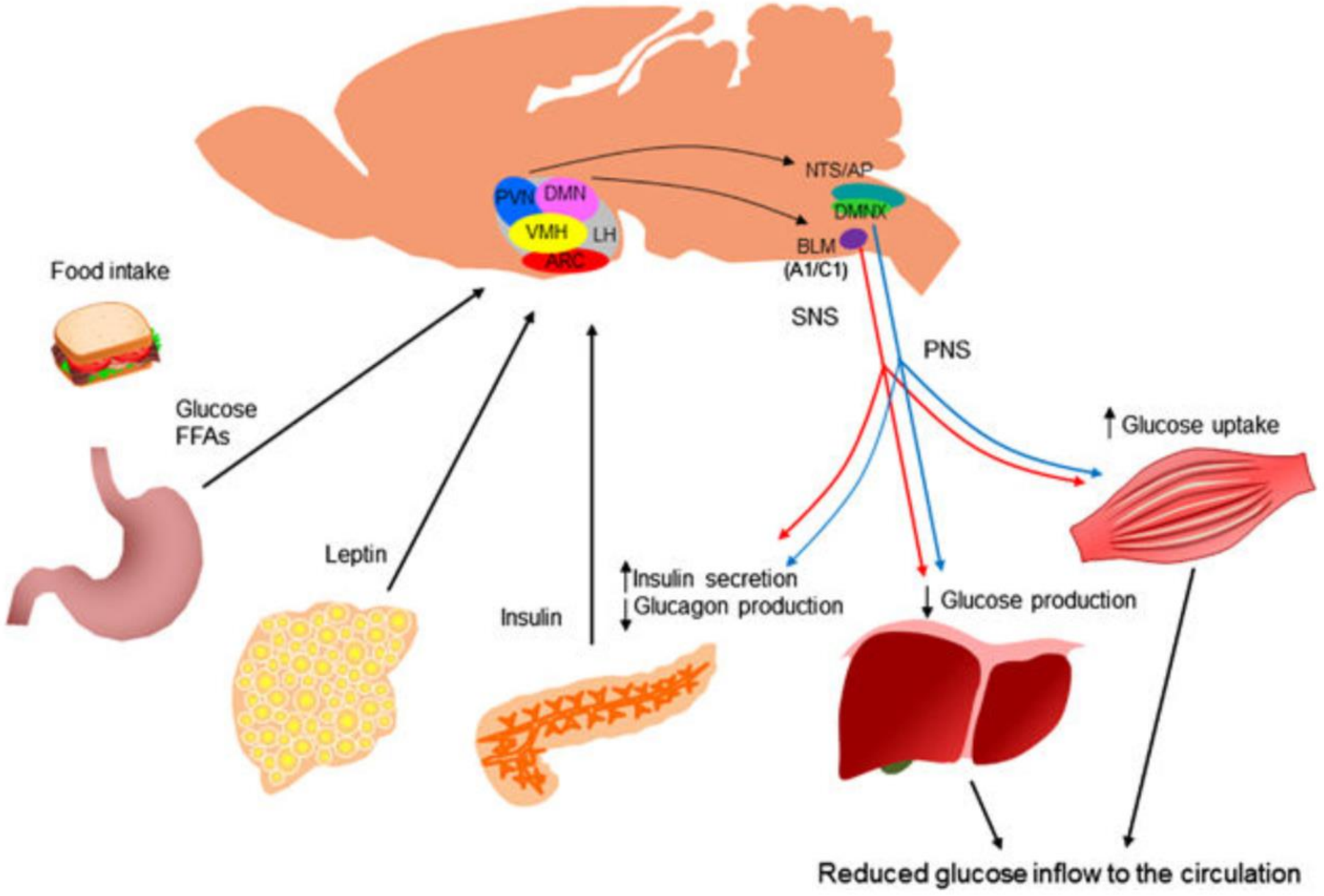
Central diabetes mellitus

Central diabetes mellitus

- Postulated mechanism
  - Hypothalamus as peripheral neuropeptide sensors to balance intake of food and energy expenditure
  - Hypothalamus as direct insulin/glucagon control
  - Dysnatremia lead to hypothalamic injury



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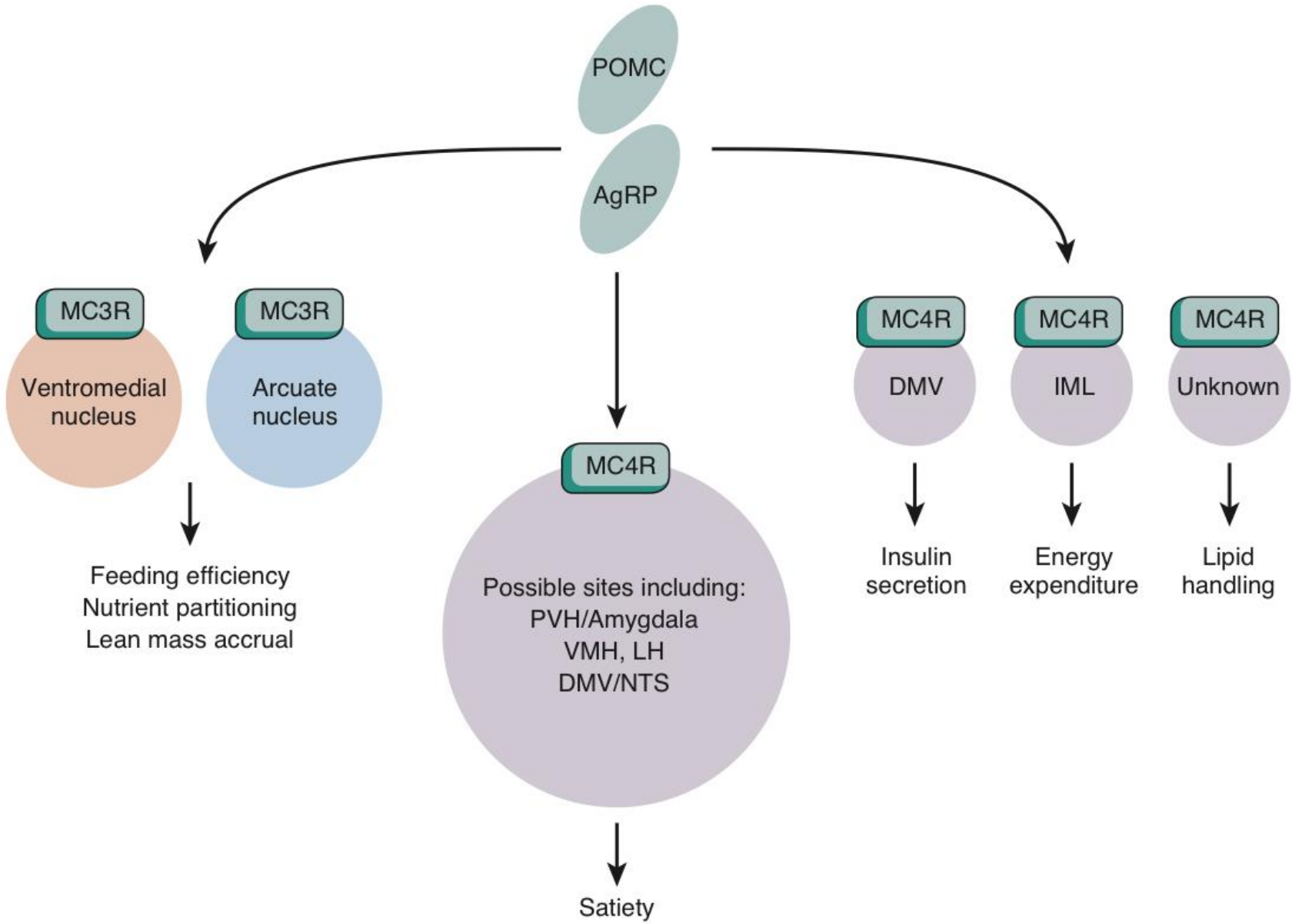

Cone RD, Elmquist JK. Neuroendocrine control of energy stores. In: Melmed S, Polonsky K, Larsen P, Kronenberg H, editors. Williams Textbook of Endocrinology. 13th ed. Elsevier Saunders, Philadelphia; 2015, p.1611-5

Central diabetes mellitus

- Dysnatremia lead to more hypothalamic injury
  - Hypernatremia can cause injury to the central nervous system
  - Case series described 11 patients who awoke from anasthesia developed spontaneous polyuria developed rapidly led to hypernatremia. Unexplained hyperglycemia was also noted. At autopsy, all patients had cerebral edema with hypoxic brain damage and 8 of 11 had hypothalamic necrosis. All had normal pancreas at autopsy.

Fracker CL, Arieff AI. Fatal central diabetes mellitus and insipidus resulting from untreated hyponatremia: a new syndrome. Ann Intern Med 1990 Jan;112(2):113-9

Case reports: Central diabetes mellitus

- HHS as presentation of hemorrhagic pituitary apoplexy[1]
- Hyperglycemia as complication after removal of large parasagittal meningioma[2]
- Hemichorea-hemiballism with HHS as presentation of GH producing pituitary macroadenoma[3]

1. Hemorrhagic pituitary apoplexy in an 18 year-old presenting as non-ketotic hyperglycemic coma (NKHC). J Pediatr Endocrinol Metab 2005 Jun; 18(6):611-5

2. Septic shock with hyperglycemia induced by hypothalamic dysfunction after removal of large parasagittal meningioma. Nagoya J Med Sci 1998 Mar; 50(1-4):9-15

3. A case report on pituitary macro adenoma presented as hemichorea hemiballism syndrome. Neurol Sci 2008 Sep;29(4):289-90

Diagnosis: Central diabetes mellitus

- The patient is not pregnant, has no history of diabetes mellitus or a family history of diabetes mellitus
- No history of use of any drug known to induce diabetes mellitus
- No use of steroid or hypertonic glucose before the onset of hyperglycemia
- Patients had fasting hyperglycemia (plasma glucose >140 mg/dl) in the absence of any causes listed other than an obvious lesion of the hypothalamus or anterior pituitary gland

Chen YL, Wei CP, Lai SM, et al. Hypothalamic Germinoma presented with Central Diabetes Mellitus and Extreme Hypernatremia: A case report. The Endocrinologist 2002;12:385-389.

Treatment

- Insulin therapy
  - Case reports; all cases developed hyperglycemic emergency during hospitalization
- Correct hypernatremia
- Treatment of hypothalamic lesion
- No available data in long term follow up

Conclusion

- Central diabetes mellitus
  - Unexplained hyperglycemia in patients with hypothalamic lesion
  - Exclude other possible causes
- Hypothalamus as part of energy and glucose control
- Temporary insulin therapy along with correction of hypernatremia
- Poor outcome was observed in all cases
  - Central diabetes and extreme hypernatremia might lead to severe brain damage

Hypothalamic Germinoma Presented With Central Diabetes Mellitus and Extreme Hypernatremia: A Case Report

Yan-Ling Chen, M.D., Chih-Peng Wei M.D.,‡ Shih-Ming Lai, M.D.,* and Tien-Chun Chang M.D.†*

Hypothalamic germinoma presenting with central diabetes mellitus and extreme hypernatremia is rare. The authors describe a 38-year-old woman with hypothalamic germinoma that manifested as recurrent attacks of nonketotic hyperosmolar hyperglycemia and extreme hypernatremia. Magnetic resonance imaging of the brain showed a hypothalamic tumor and a normal pituitary gland. Examination of endocrine function revealed hypogonadism and hyperprolactinemia. DDAVP test showed central diabetes insipidus. She was treated with tumor debulking and radiotherapy. The glucose level became normal and no more hypoglycemic agent was needed. However, hyperglycemia was noted again 2 months after discharge, with recurrent nonketotic hyperosmolar hyperglycemia and associated hypernatremia. She died at home suddenly 11 months after the diagnosis. Although the survival rate of hypothalamic germinoma is 87.5% over the course of 10 years, symptoms of central diabetes mellitus and extreme hypernatremia may represent a poor prognosis. ■

The Endocrinologist 2002; 12: 385–389

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Hypothalamic Germinoma Presented With Central Diabetes Mellitus and Extreme Hypernatremia: A Case Report

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A 38-year-old woman presented with muscle weakness and confusion

1 year history of polyuria and polydipsia
OGTT: normal

PE: No focal neurodeficit

Plasma glucose 592 mg/dl Cr 1.1 mg/dl
Na 184 mmol/l, K 4.2 mmol/l
HCO3 38.1
pH (ABG): 7.46
Serum ketone negative

The Endocrinologist 2002; 12: 385–389

Diagnosis: HHS

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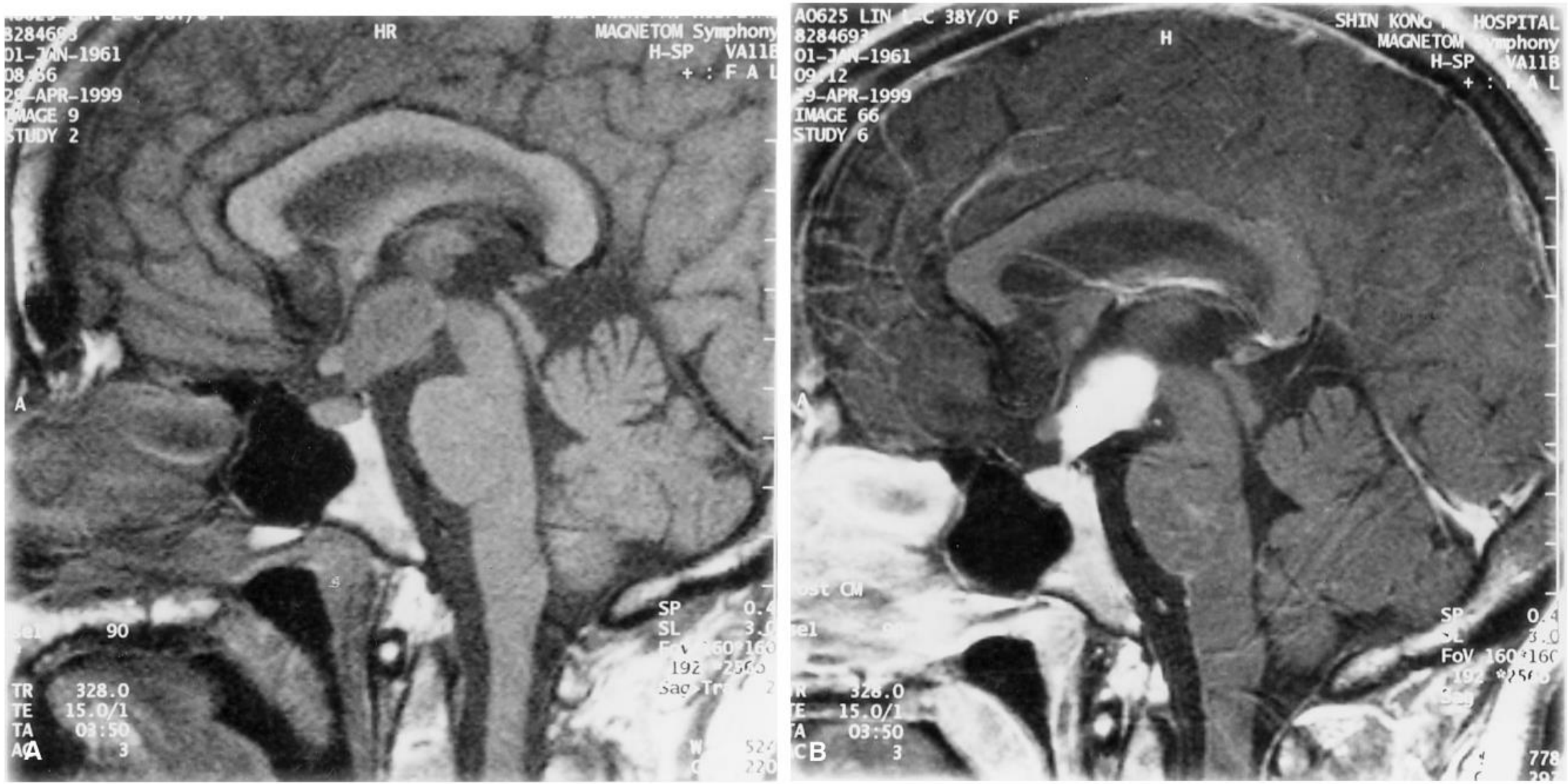

Figure 1. Sagittal section of T1- weighted magnetic resonance images of brain showing a hypothalamic germinoma with thickening of pituitary stalk . **A.** Unenhanced. **B.** After gadolinium enhancement and changes 9 months after operation and radiotherapy. **C.** Unenhanced. **D.** After gadolinium enhancement.

Component	Plasma concentration (normal range)
Prolactin (μg/L)	133.82 (0–20)
FSH (mIU/mL)	1.65 (3.85–8.78)
LH (mIU/mL)	0.2 (2.12–10.89)
Estradiol (pg/mL)	<10 (10–50)
Cortisol 8:00 AM (μg/dL)	8.18 (7–25)
ACTH 8:00 AM (pg/mL)	10.7 (9–52)
Growth Hormone (ng/mL)	0.31 (0–5)
T_4 (μg/dL)	5.6 (4.5–12)
T_3 (ng/dL)	97.83 (80–180)
TSH (μU/mL)	2.15 (0.4–5.0)

DDAVP 10ug IV
Urine osm. 303->723

	0 minute	15 minutes	30 minutes	60 minutes	120 minutes
LHRH test (100 μg LHRH intravenous injection)					
LH (mIU/mL)	<0.2	0.59	0.92	1.19	2.23
FSH (mIU/mL)	1.57	1.93	5.38	6.0	8.25
TRH test (400 μg TRH intravenous injection)					
TSH (μU/mL)	2.84	24.56	36.01	32.93	23.42
Prolactin	126.11	358.01	186.93	186.28	144.26
ITT (0.35 U/kg insulin intravenous injection)					
Glucose (mg/dL)	153	107	145	135	247
Cortisol (μg/dL)	2.2	2.24	2.93	4.9	9.68
GH (ng/mL)	0.31	0.23	0.41	0.49	0.33

LHRH, LH-releasing hormone; TRH, TSH-releasing hormone; ITT, insulin tolerance test; GH, growth hormone.

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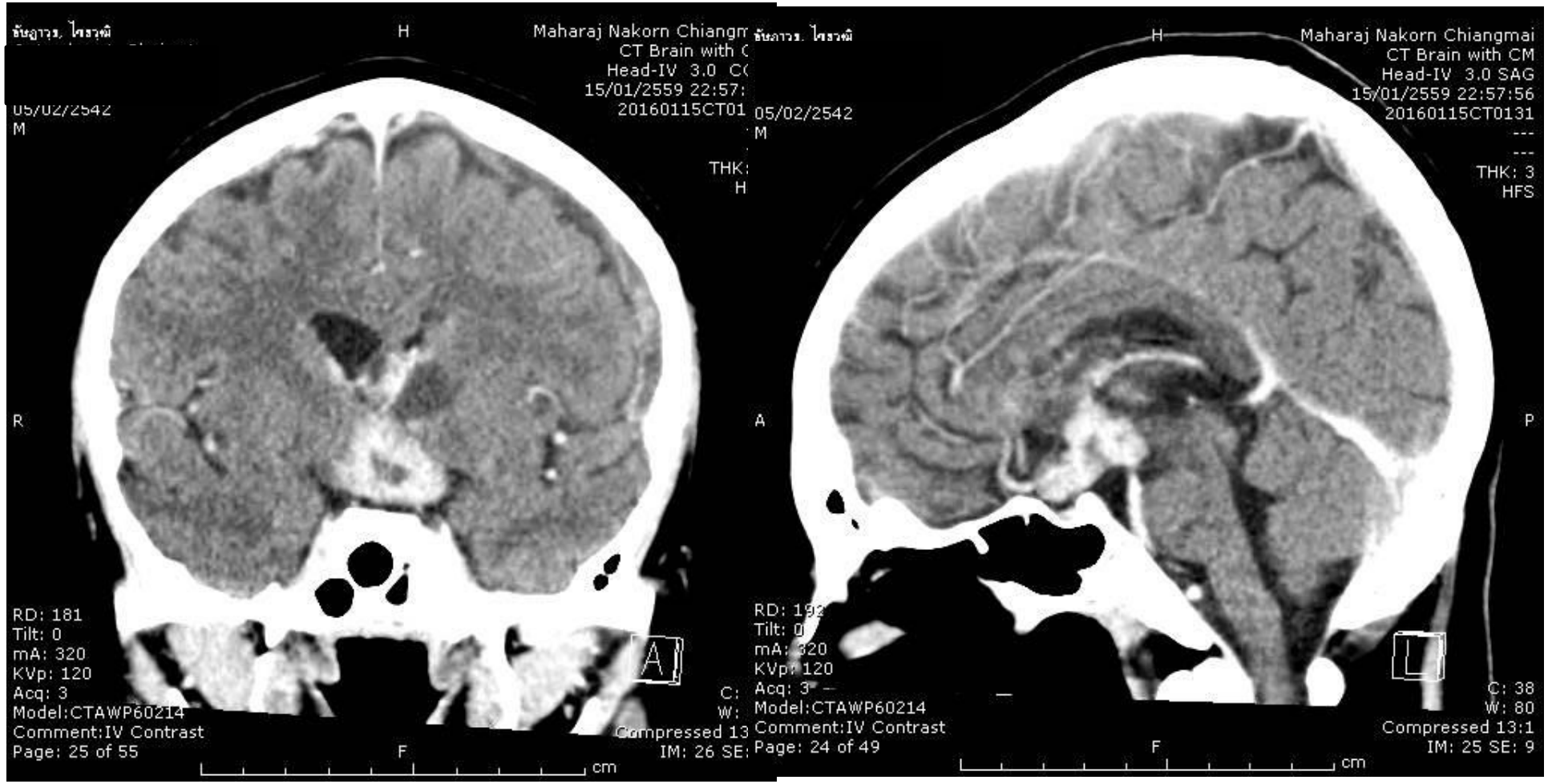
Case report:
Central diabetes mellitus

- Hyperglycemia: HHS
  - Insulin therapy 40 units/day then taper off in 42 days
  - C-peptide level: 6.2 ng/ml
  - HbA1C 7.3%
- Hypothalamic germinoma
  - Radiotherapy
- Hypopituitarism with central DI
  - Glucocorticoid, thyroid hormone and DDAVP

Chen YL, Wei CP, Lai SM, et al. Hypothalamic Germinoma presented with Central Diabetes Mellitus and Extreme Hypernatremia: A case report. The Endocrinologist 2002;12:385-389.

Another CMU hospital cases

- A 18-year-old boy
- Basal ganglia and suprasellar germinoma,
  - Presented with progressive headache and vertigo for a year S/P frontotemporal craniotomy to remove tumor
- Pathologic diagnosis: germinoma (+ CD117)
  - Serum α-fetoprotein :1.62 IU/ml (normal:0-11.29) and serum β-human chorionic gonadotropin below 0.1 mIU/mL (normal: <1.0)
- Delayed puberty from physical examination, other pituitary hormone assay confirmed central diabetes insipidus, central hypothyroid and central adrenal insufficiency
- Poor compliance with DDAVP, he developed hypernatremia with serum sodium of 164 mmol/L -> admit for reevaluation and DDAVP dose adjustment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Another CMU hospital cases

- Initial laboratory tests
  - BUN 22 mg/dL, Cr 1.2 mg/dL, Na 164 mmol/L, K 3.9 mmol/L, Cl 121 mmol/L, HCO3 27 mmol/L
  - UA: urine sp.gr 1.007 , albumin negative, sugar 4+ (no blood sugar measurement at that time)
- 1 week after admission, he was drowsy. plasma glucose: 1,005 mg/dl with Na 170 mmol/L, HCO3 18 mmol/L, pH (ABG) 7.34, serum ketone negative —> HHS
- No history of diabetes mellitus and family history of diabetes
- HbA1C was 8.29%
- Insulin treatment 40 units/day. 10 days after HHS diagnosis, glycemic level was controlled and insulin treatment was tapered off

	Chen YL. et al	CMU hospital Case 1	CMU hospital Case 2
Sex/Age	38-year-old woman	19-year-old girl	18-year-old boy
Type of hypothalamic lesion	Hypothalamic germinoma	Hypothalamic germinoma	Basal ganglia and hypothalamic germinoma
Anterior pituitary hormone deficiency	GH deficiency Central AI Central hypothyroidism HH	Central AI Central hypothyroidism HH	Central AI Central hypothyroidism suspected HH
Central DI	Adipsic DI	Adipsic DI	Adipsic DI
Hyperglycemic emergency	Presentation as HHS	HHS during work up	HHS during treatment

	Chen YL. et al	CMU hospital Case 1	CMU hospital Case 2
FH of diabetes	No	No	No
HbA1C at time of HHS	7.3%	6.2%	8.3%
C-peptide	6.2 ng/mL	NA	NA
Glucocorticoid treatment before HHS	NA	15 mg/day of prednisolone	5 mg of prednisolone
Rate of dextrose infusion before HHS	NA	5 gm/hour	4 gm/hour
Insulin requirement/day	40 units	20 units (0.5 unit/kg/day)	40 units (0.6 unit/kg/day)
Duration of insulin	42 days	22 days	10 days
Outcome	Dead	Dead due to sepsis	Loss to follow up