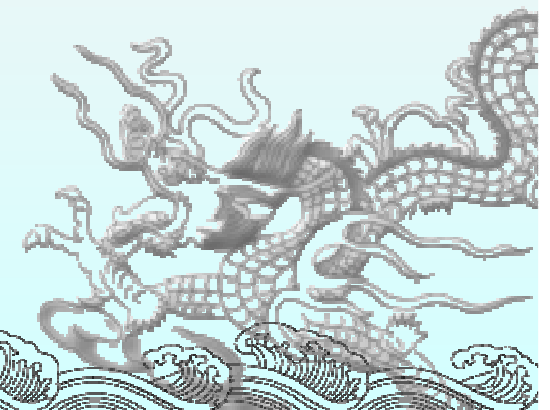
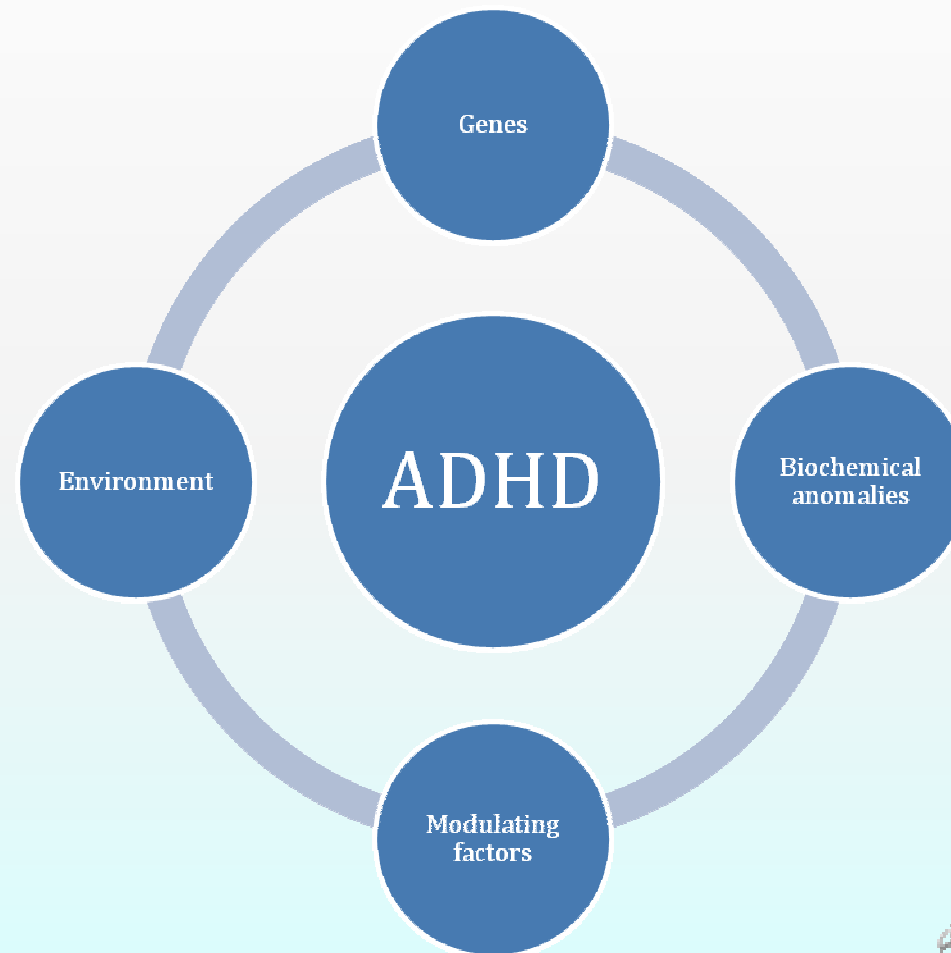


Attention-Deficit / Hyperactivity Disorder: Challenges to Clinicians

Dr. C. P. Tang



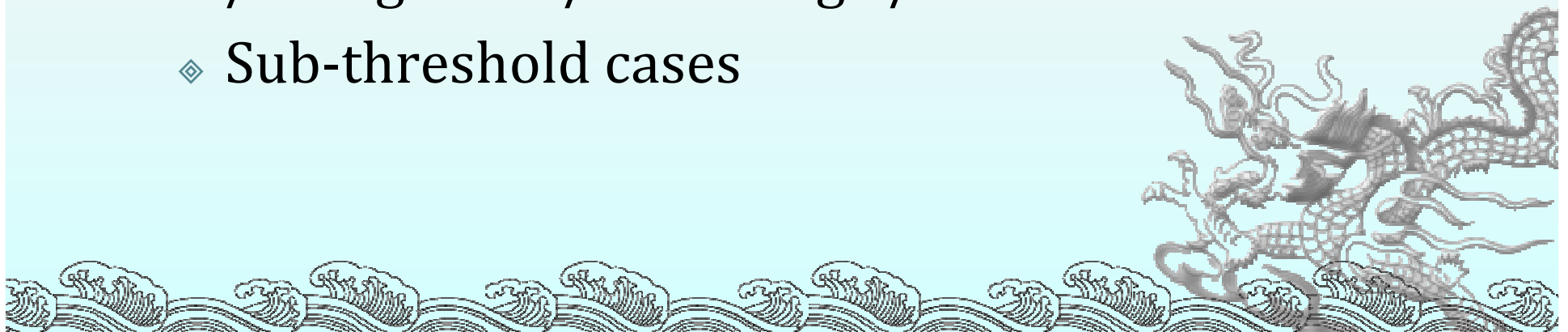
A highly prevalent and complex disorder with multiple causes



Diagnostic challenges - 1

- ◆ **A syndromal diagnosis**

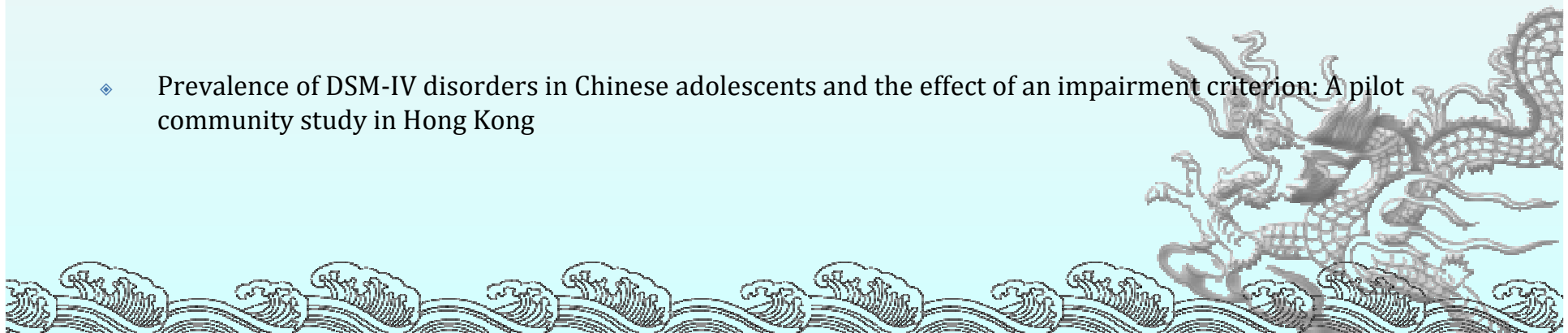
- ◆ 6/9 inattention + 6/9 overactivity/impulsivity symptoms, ≥ 6 months, ≥ 2 situations, impairment
- ◆ ? Cut-off
- ◆ Subjected to informant's expectation /background/knowledge /mental state
- ◆ Sub-threshold cases



- ◆ Prevalence study, Chinese, grade 7-9, DISC-IV

- ◆ N=541 (261 boys, 280 girls)
- ◆ Symptom criteria = 4.4% (5.7%, 3.2%)
- ◆ + Impairment criteria = 3.9% (5.4%, 2.5%)
- ◆ % reduction in prevalence = 11% (5%, 21%)

- ◆ Prevalence of DSM-IV disorders in Chinese adolescents and the effect of an impairment criterion: A pilot community study in Hong Kong

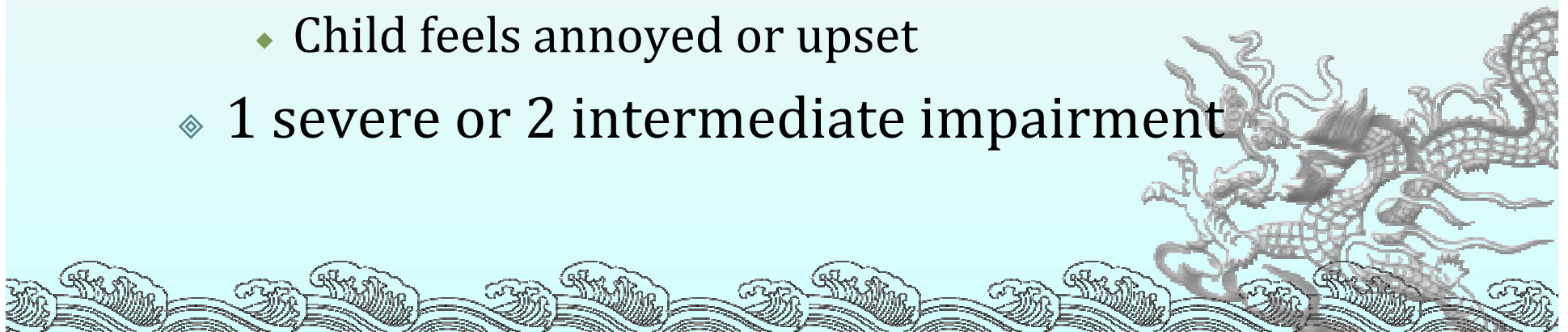


◆ Impairment criteria

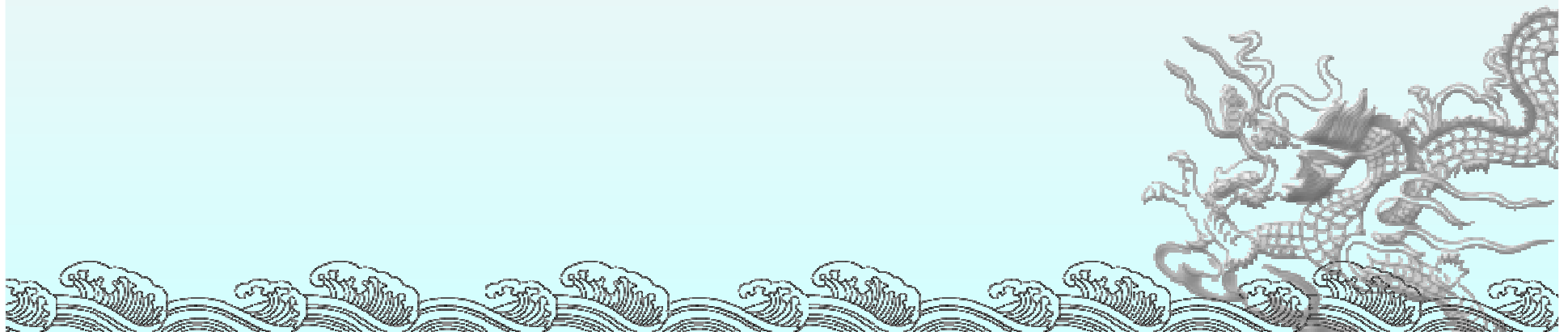
◆ 6 domains of daily living

- ◆ Caretakers get annoyed or upset
- ◆ Doing things / going places with family
- ◆ Doing things / going places with friends
- ◆ Schoolwork or grade
- ◆ Teachers get annoyed or upset
- ◆ Child feels annoyed or upset

◆ 1 severe or 2 intermediate impairment

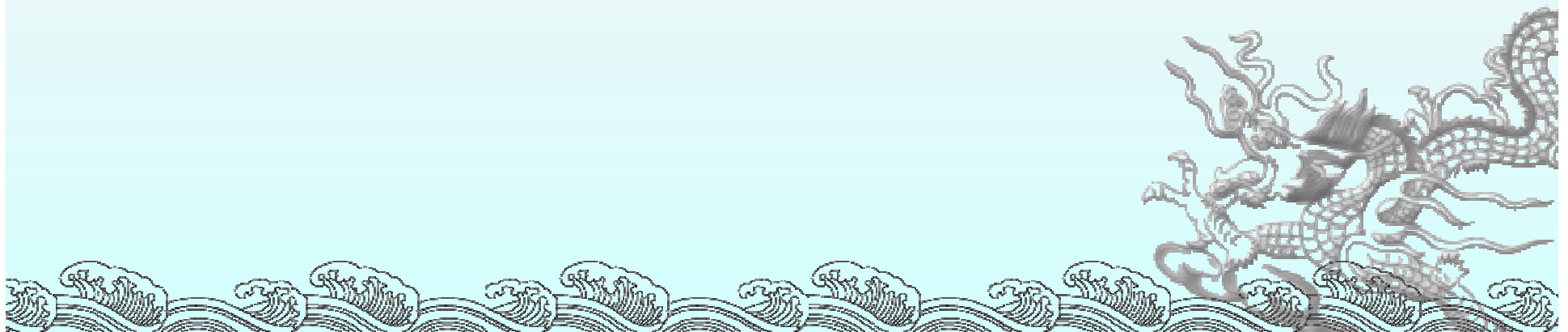


-
- ◆ No laboratory or radio-imaging diagnostic test



Diagnostic challenges - 2

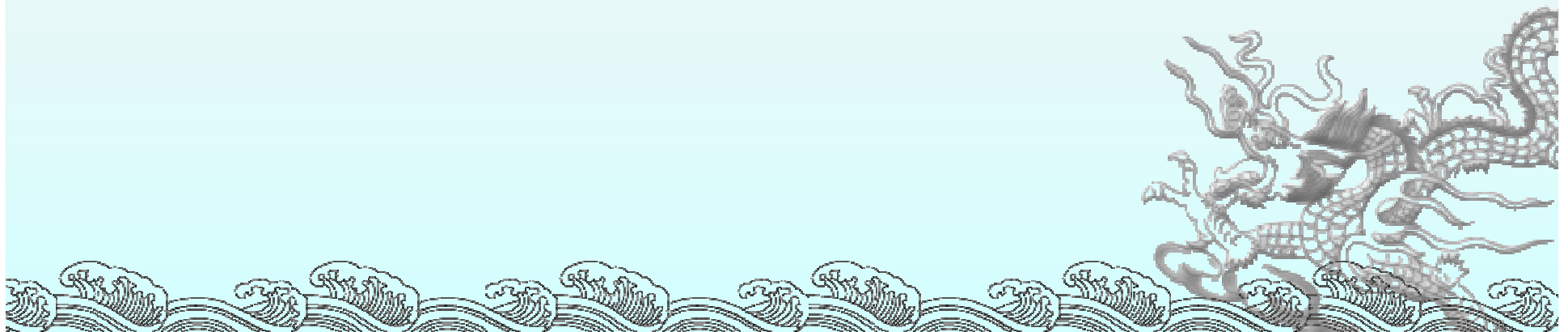
- ◆ **Poor consistency among informants**
 - ◆ Poor correlation between parent ratings and teacher ratings
 - ◆ Similar discrepancy between child and adult
 - ◆ Cultural / mindset variables
 - ◆ ASEBA



Diagnostic challenges - 3

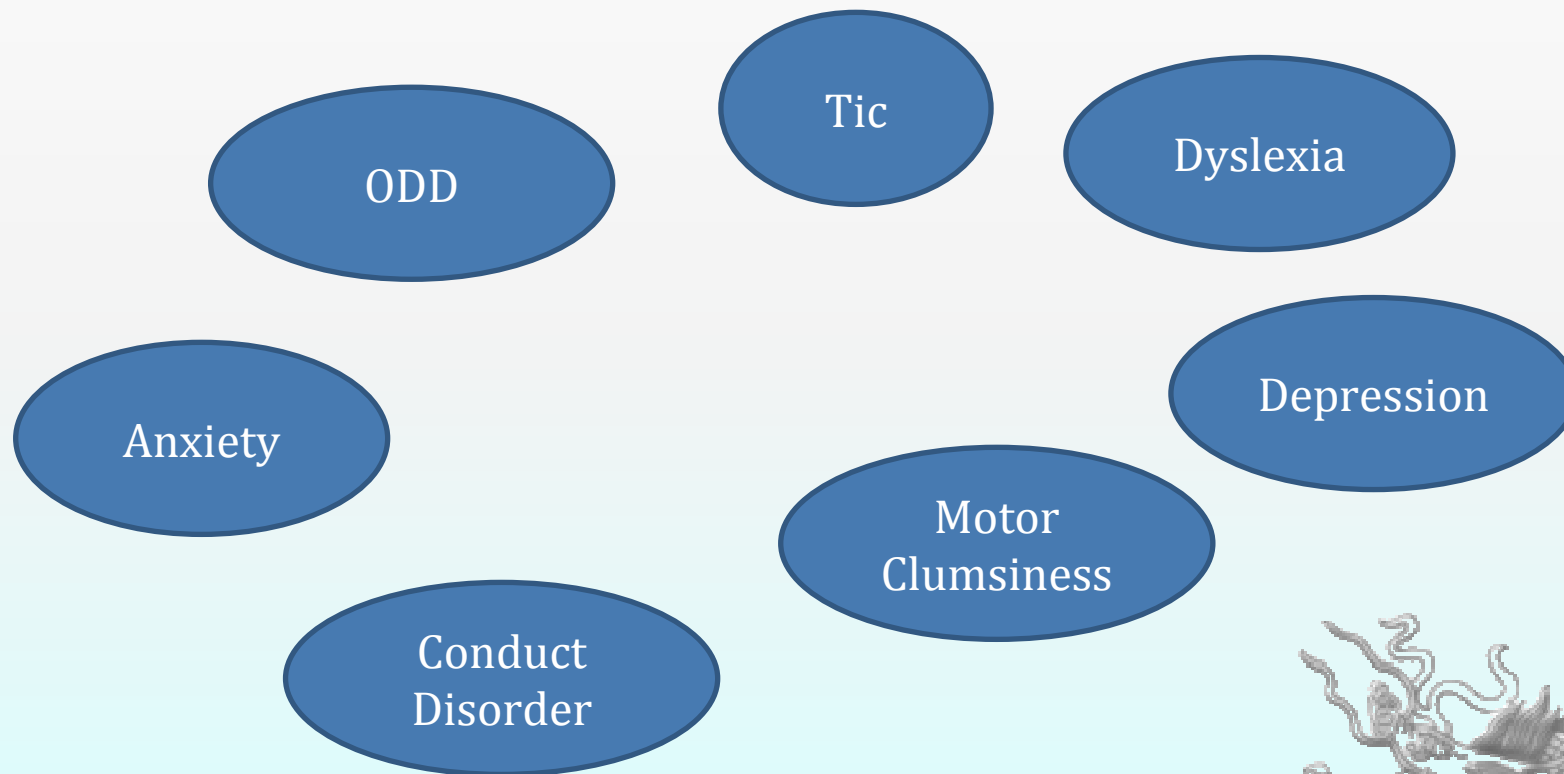
- ◆ **Differential diagnoses**

- ◆ May get confused with other conditions e.g. ODD, learning difficulty, cognitive deficiency, anxiety disorders, bipolar affective disorder



Diagnostic challenges - 4

◆ High comorbidities



Treatment challenges - 1

- ◆ Limited choice / availability of effective treatment
 - ◆ Most HA pharmacy provide only Ritalin ± Concerta / Strattera as 1st line medication treatment
 - ◆ Psycho-social treatment program
 - ◆ School based support and intervention



Treatment challenges - 2

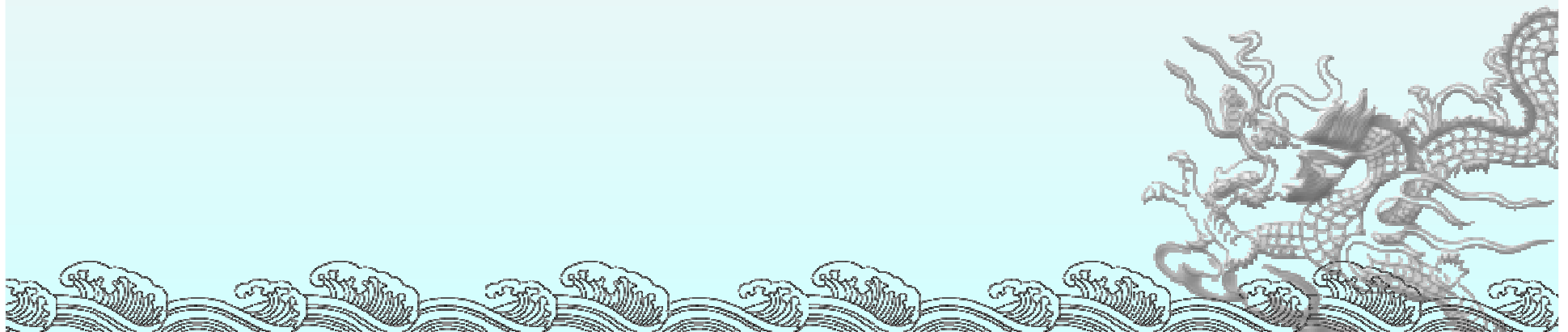
- ◆ Long term benefit of medication treatment
 - ◆ Superiority over non-medicated comparison groups reduce at 24 months and almost disappear at 36 months

- ◆ Peter S Jensen et al. 3-year follow up of the NIMH MTA Study. J. Am. Acad. Child Adolesc. Psychiatry, 46:8, August 2007



Treatment challenges - 3

- ◆ Adverse effect or long term hazards associated with medication treatment

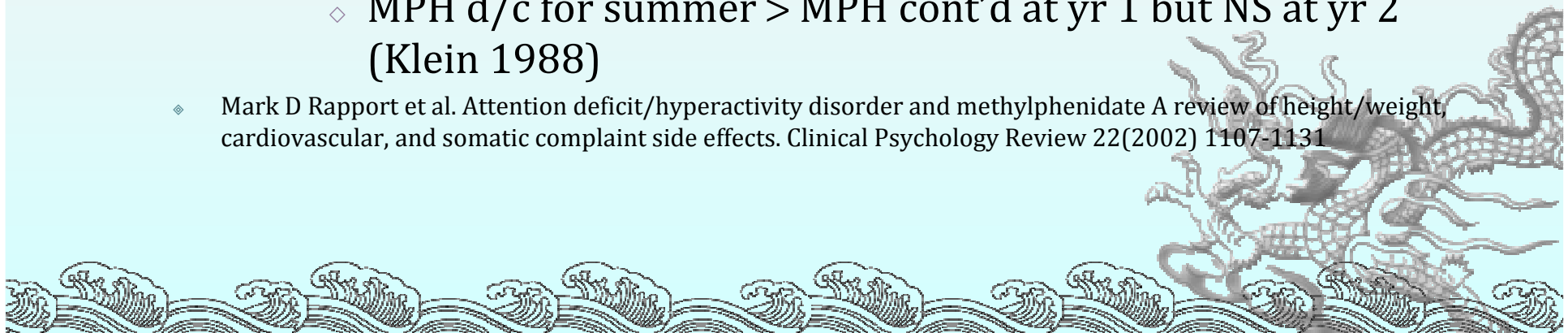


◆ Growth suppression

◆ Weight

- ◆ 8/11 studies reported significant differences,
 - ◆ 20mg MPH > 30-40 mg; Ss cont'd thro' summer < Ss d/c (Safer 1972)
 - ◆ MPH < expected at yr 1 & 2; Ss cont'd thro' summer < Ss d/c (Scatterfield 1979)
 - ◆ Placebo > MPH (Conners 1980)
 - ◆ MPH (%tile) < baseline after 1-4 years; does related (Mattes 1983)
 - ◆ MPH d/c for summer > MPH cont'd at yr 1 but NS at yr 2 (Klein 1988)

- ◆ Mark D Rapport et al. Attention deficit/hyperactivity disorder and methylphenidate A review of height/weight, cardiovascular, and somatic complaint side effects. Clinical Psychology Review 22(2002) 1107-1131



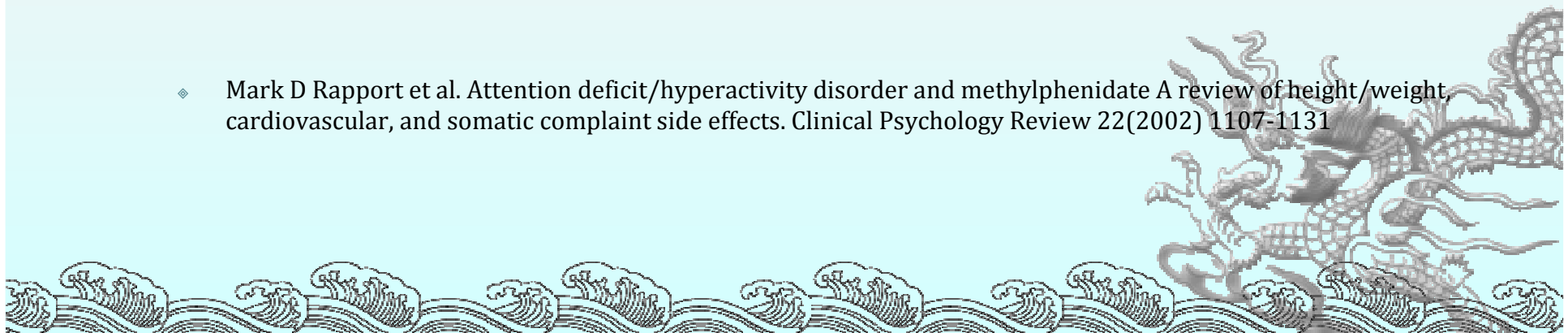
◆ Growth suppression

◆ Height

◆ 4/10 studies reported significant findings

- ◆ MPH (%tile) < control (Safer 1972)
- ◆ MPH (%tile) < baseline after 2-4 years, dose related (Mattes 1983)
- ◆ MPH < expected at yr1 but NS at yr 2 (Scatterfield 1979)
- ◆ MPH cont'd thro' summer < d/c at yr 2 (Klein 1988)

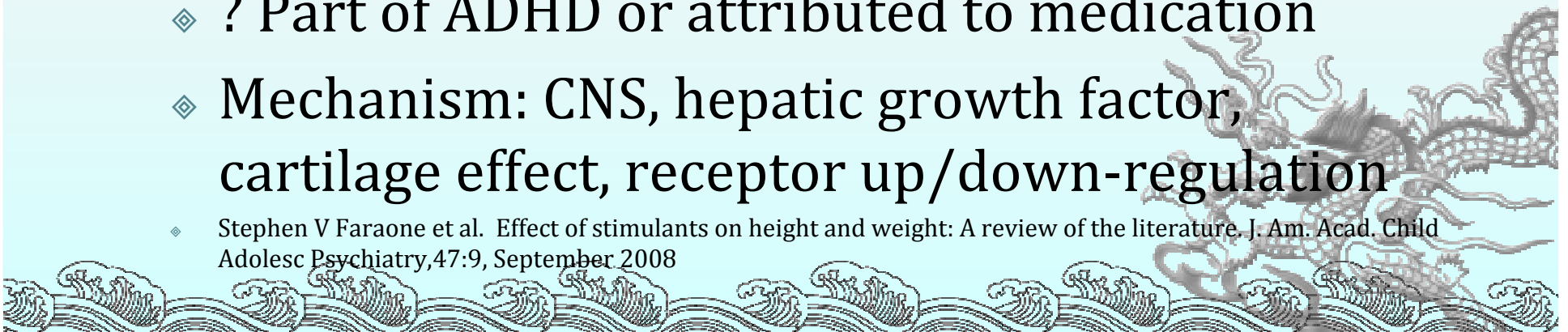
- ◆ Mark D Rapport et al. Attention deficit/hyperactivity disorder and methylphenidate A review of height/weight, cardiovascular, and somatic complaint side effects. Clinical Psychology Review 22(2002) 1107-1131



◆ Growth suppression

- ◆ Stimulant medications lead to delays in expected growth in height and weight
- ◆ Most obvious in the heavier and taller (vs light & short) children (vs adolescent)
- ◆ Ht & wt deficits increase with length of time on medication
- ◆ Deficits attenuate over time (even if maintained on medication)
- ◆ ? Part of ADHD or attributed to medication
- ◆ Mechanism: CNS, hepatic growth factor, cartilage effect, receptor up/down-regulation

◆ Stephen V Faraone et al. Effect of stimulants on height and weight: A review of the literature. J. Am. Acad. Child Adolesc Psychiatry, 47:9, September 2008

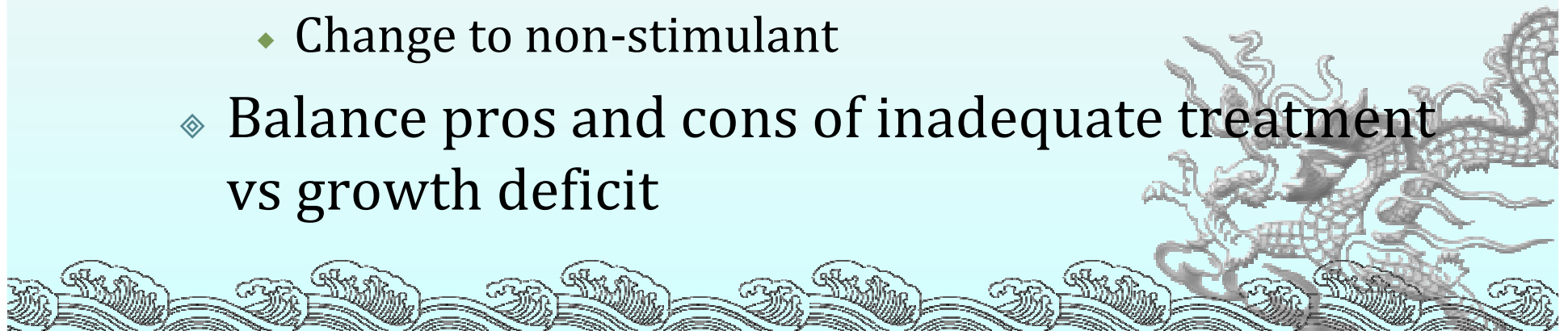


◆ Growth suppression

◆ Management strategies:

- ◆ Explanation, education & explore expectation
- ◆ Monitoring
- ◆ Adjustment in dose regimen
- ◆ Meal arrangement
- ◆ Drug holiday
- ◆ Change to non-stimulant

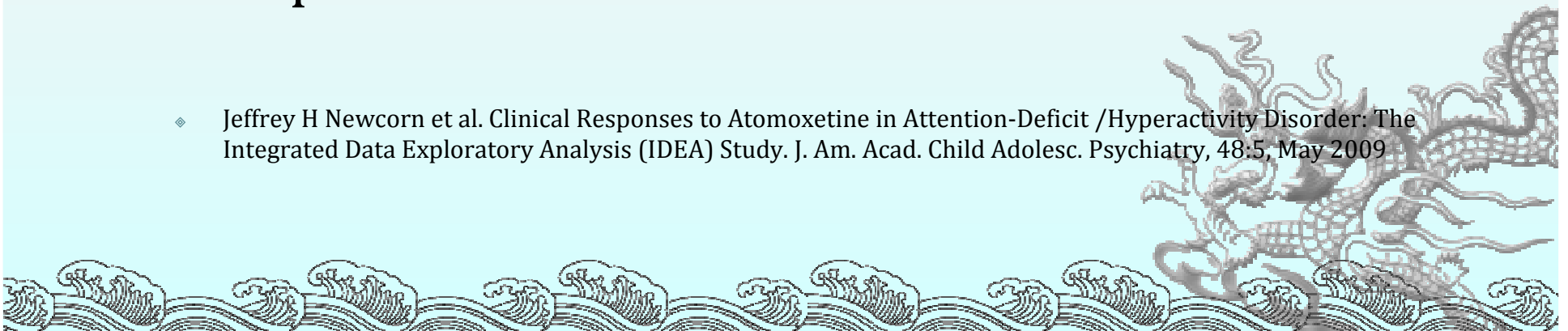
◆ Balance pros and cons of inadequate treatment vs growth deficit



◆ Tic

- ◆ Worsening by stimulant?
- ◆ Clonidine and Atomoxetine significantly improve comorbid tic symptoms
- ◆ Methylphenidate does not associate with worsening of tic. Some suggestion that they may improve tic

◆ Jeffrey H Newcorn et al. Clinical Responses to Atomoxetine in Attention-Deficit /Hyperactivity Disorder: The Integrated Data Exploratory Analysis (IDEA) Study. J. Am. Acad. Child Adolesc. Psychiatry, 48:5, May 2009

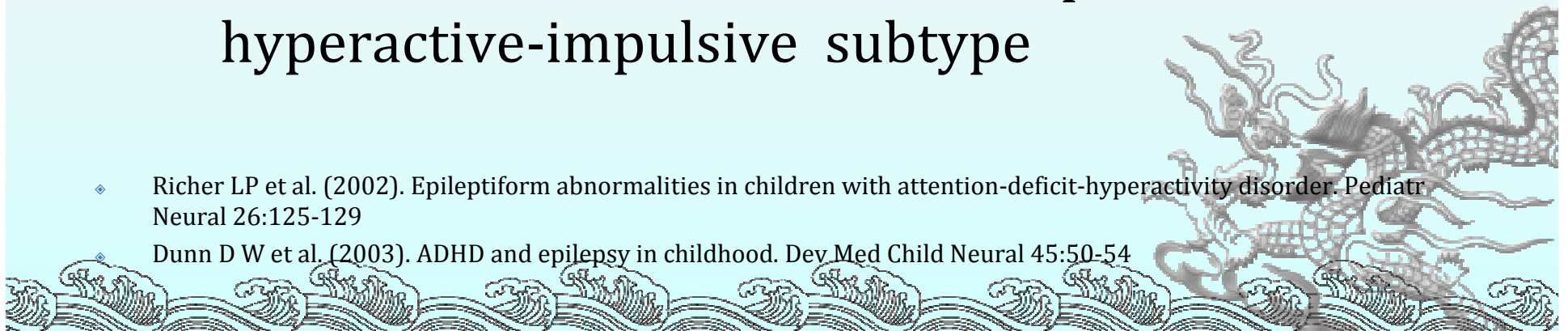


◆ Seizure

- ◆ Comorbidity of seizure & ADHD greater than expected
- ◆ ↑Risk for EEG abnormalities in ADHD children (6.1% vs, 3.5%) and subsequent seizure
- ◆ In a group of Pediatric epileptic patient (n=175) 24% meet ADHD pred inattentive criteria, 11% for ADHD combined, and 2% for pred hyperactive-impulsive subtype

◆ Richer LP et al. (2002). Epileptiform abnormalities in children with attention-deficit-hyperactivity disorder. *Pediatr Neural* 26:125-129

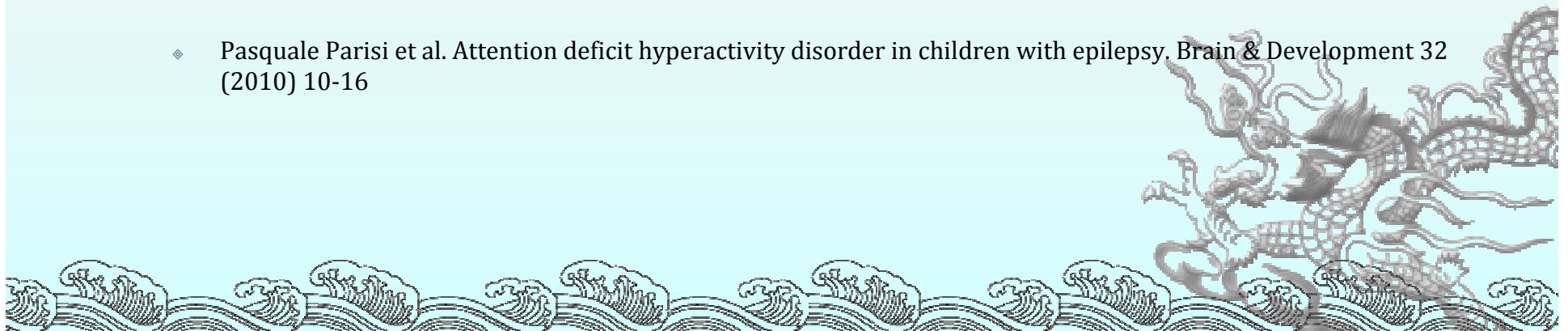
Dunn D W et al. (2003). ADHD and epilepsy in childhood. *Dev Med Child Neural* 45:50-54



◆ Seizure

- ◆ Some AED may exacerbate behavioral symptoms (e.g. barbiturates, topiramate)
- ◆ Consider valporate , carbamazepine (improve mood & beh problems), levetiracetam , lamotrigine, clobazam (does not impair cognitive/executive function)

- ◆ Pasquale Parisi et al. Attention deficit hyperactivity disorder in children with epilepsy. Brain & Development 32 (2010) 10-16



◆ Seizure

- ◆ Some ADHD medications may lower seizure threshold
- ◆ Case report about new onset seizure in MPH treated patient
- ◆ Improve ADHD symptoms in controlled trials of MPH in epileptic patients
- ◆ In a recent meta-analysis, seizure risk in medicated (MPH, atomoxetine) ADHD patients is not statistically different from placebo or population seizure risk

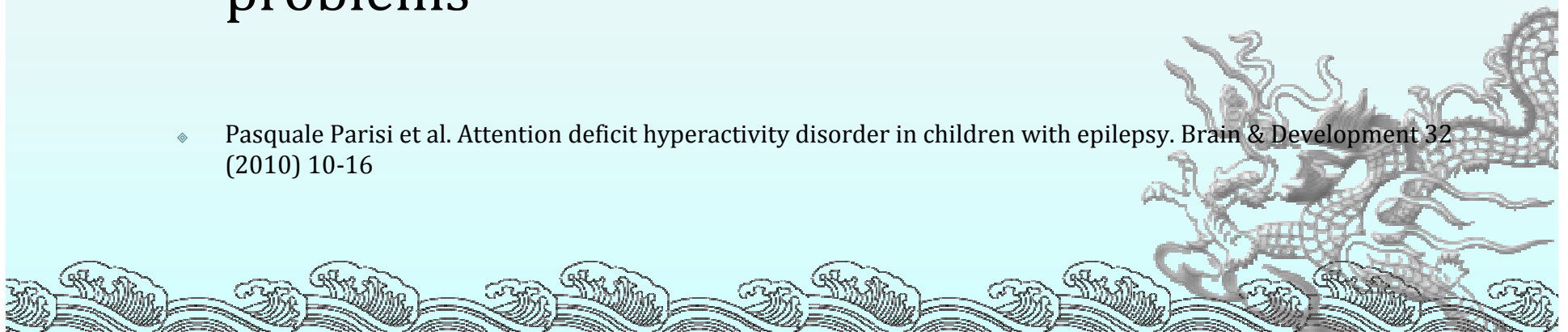
◆ Pasquale Parisi et al. Attention deficit hyperactivity disorder in children with epilepsy. *Brain & Development* 32 (2010) 10-16

◆ Joachim F Wernicke et al. Seizure risk in patients with attention-deficit-hyperactivity disorder treated with atomoxetine. *Developmental Medicine and Child Neurology*, London: Jul 2007, Vol 49, Iss 7; pg 498.

◆ Seizure

- ◆ MPH or atomoxetine if the ADHD s/s $\geq$ moderate + seizure $\leq$ once/month
- ◆ 2nd line: trial of clonidine or guanfacine
- ◆ 3rd line: TCA or modafinil
- ◆ Melatonin may be considered for sleep problems

- ◆ Pasquale Parisi et al. Attention deficit hyperactivity disorder in children with epilepsy. *Brain & Development* 32 (2010) 10-16

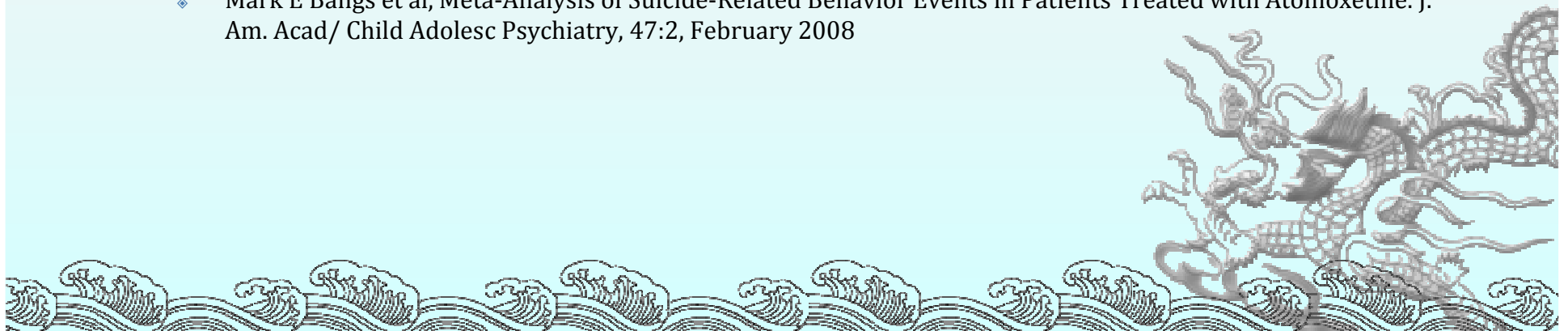


◆ Suicide behavior

◆ Meta-analysis

- ◆ Suicidal-related behavior
- ◆ 0.37% (5/1357) in Atomoxetine group vs. 0% in placebo group
- ◆ Nil committed suicide

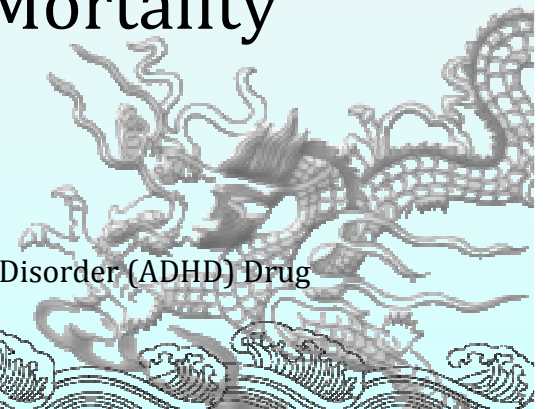
- ◆ Mark E Bangs et al, Meta-Analysis of Suicide-Related Behavior Events in Patients Treated with Atomoxetine. J. Am. Acad/ Child Adolesc Psychiatry, 47:2, February 2008



◆ Sudden death

- ◆ FDA review (2006) of isolated reports of sudden death (19 under 18-year-old, 6 adult cases) in patients taking medications to treat ADHD ⇒ inconclusive
- ◆ Retrospective cohort study (2009) identify 7 cases of death from 18637 patient-year (1993-2006) who were prescribed methylphenidate, dexamfetamine, and Atomoxetine. Mortality rate similar to general population

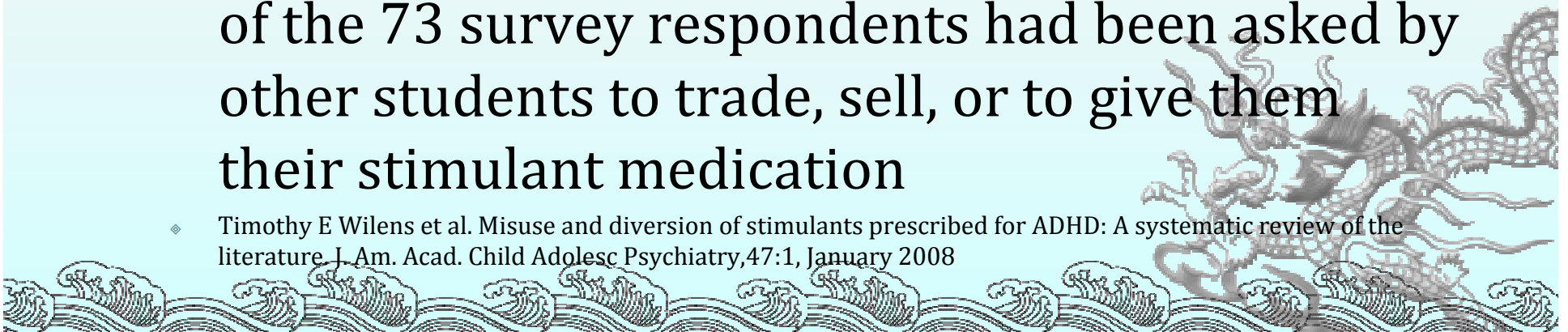
◆ Suzanne McCarthy et al. Mortality Associated with Attention-Deficit Hyperactivity Disorder (ADHD) Drug Treatment. *Drug Saf* 2009;32(11):1089-1096



◆ Drug abuse / addiction

- ◆ Controversy
- ◆ Stay awake for studying/exam
- ◆ Misuse & diversion
- ◆ A review (21 studies, 113,145 subjects) found 5-9% past year prevalence of stimulant misuse in grade/high-school-age children (5-35% in college students)
- ◆ A study of 161 students on MPH found that 16% of the 73 survey respondents had been asked by other students to trade, sell, or to give them their stimulant medication

◆ Timothy E Wilens et al. Misuse and diversion of stimulants prescribed for ADHD: A systematic review of the literature. J. Am. Acad. Child Adolesc Psychiatry, 47:1, January 2008



◆ Drug abuse / addiction

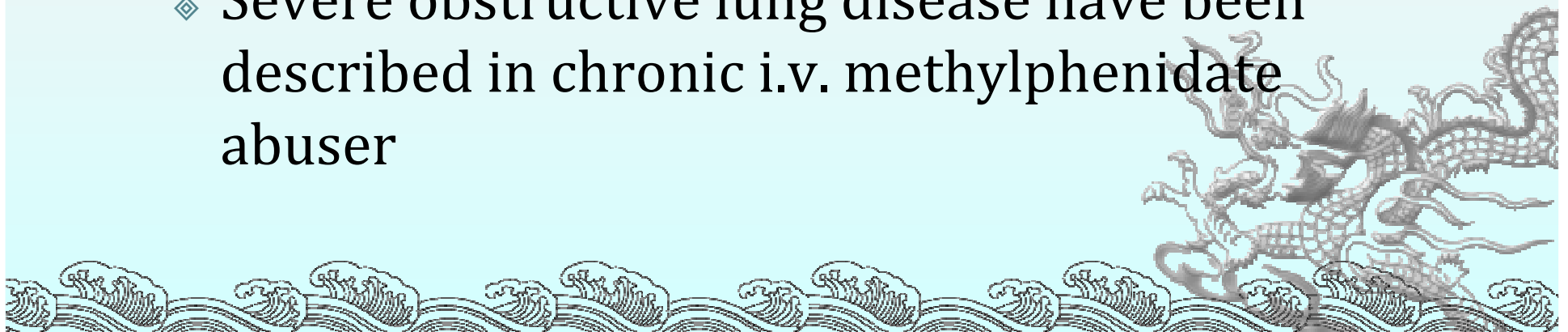
- ◆ Men reports more misuse
- ◆ White and Hispanics 3× the rate in African American and 2 × the rate in Asian American (Teter 2006)
- ◆ Motivation: to concentrate (58%), alertness (43%), get 'high' (43%), others (14%) (Teter 2005)
- ◆ Oral (96%), intra-nasal (38%) (Teter 2006)
- ◆ Comorbid with CD &/or SA
 - ◆ Divert (83% had CD, 83% had SA)
 - ◆ Misuse (58% had CD, 75% had SA)

- ◆ Timothy E Wilens et al. Misuse and diversion of stimulants prescribed for ADHD: A systematic review of the literature. J. Am. Acad. Child Adolesc Psychiatry, 47:1, January 2008



- ◆ Drug abuse / addiction

- ◆ “Vitamin R”, “R-ball”, “Skippy”
- ◆ Oral /snorting /i.v.
- ◆ Toxic effects: irritability, agitation, euphoria, lethargy, dizziness, restlessness, hallucination, delusion, seizure; tachycardia, hypertension, arrhythmia, vomiting, abd pain
- ◆ Withdrawal s/s: lethargy, apathy, depression, paranoid
- ◆ Severe obstructive lung disease have been described in chronic i.v. methylphenidate abuser



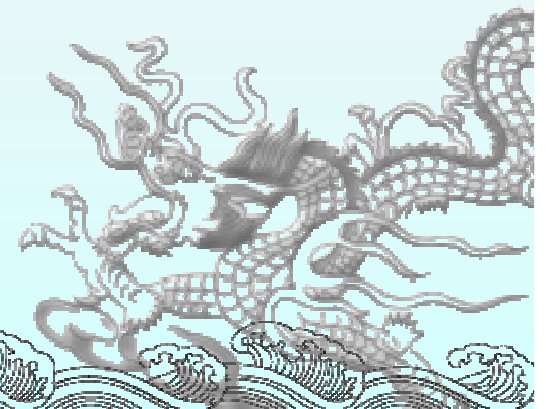
◆ Drug abuse / addiction

◆ DDx: intoxication with other substances

◆ Management:

- ◆ Activated charcoal
- ◆ Agitation
- ◆ Delirium
- ◆ Seizure
- ◆ Psychotic symptoms
- ◆ Arrhythmia
- ◆ Hypertension
- ◆ Fever

◆ Prevention



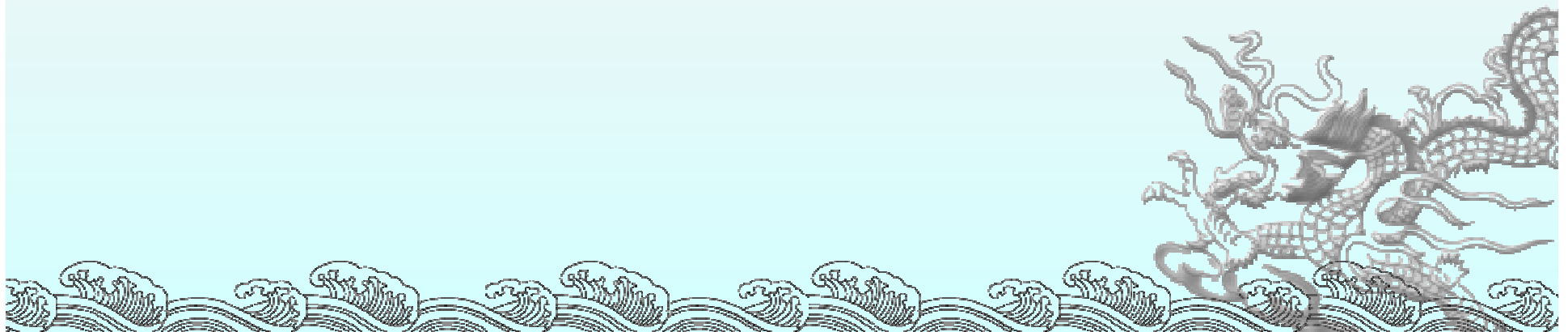
Treatment challenges - 4

- ◆ Compliance problem
 - ◆ Irregular drug intake
 - ◆ Over use of drug holiday
 - ◆ Premature drop out of treatment
 - ◆ More of a problem if comorbid with ODD, CD, familial psychopathology, inadequate parental supervision



Treatment challenges - 5

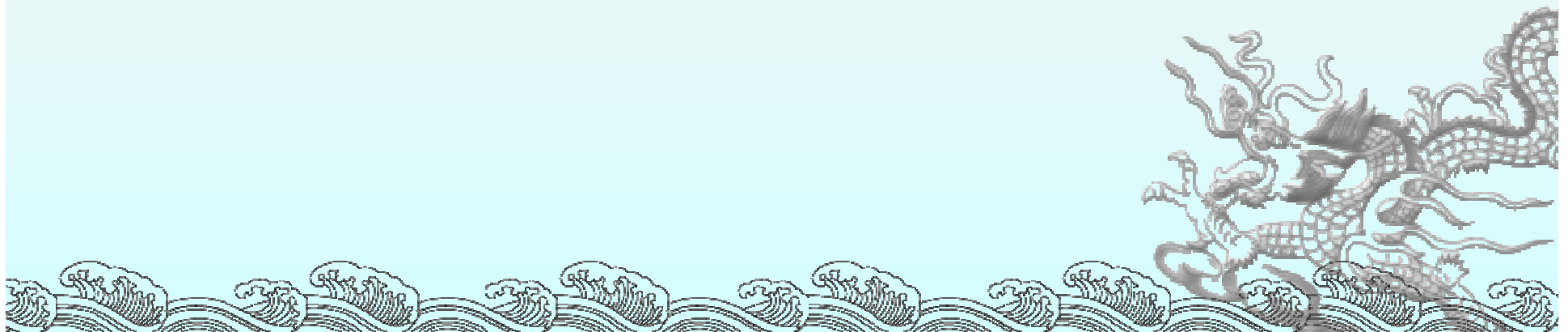
- ◆ Expectation from patient /family
 - ◆ Increase service demand
 - ◆ Ready availability of ADHD information over the web / media (some are misleading)
 - ◆ Reduced reserve /functions of the family



Treatment challenges - 6

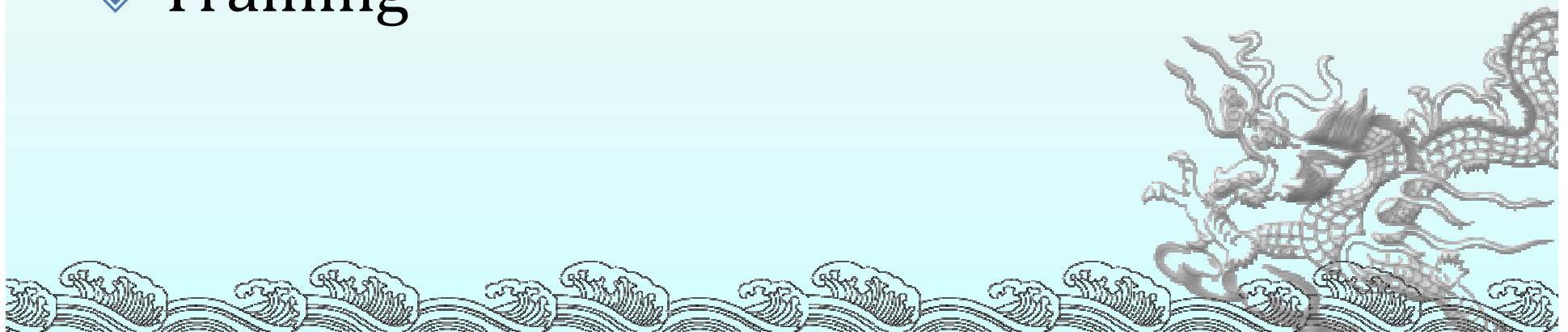
◆ Continuity of care

- ◆ A developmental problem which commonly extends into adult life
- ◆ Transition to adult service
- ◆ Expertise and availability of adult assessment & treatment service



The way ahead

- ◆ Increase demand
- ◆ Limited resource
- ◆ Restructuring of service provision
- ◆ Set priority
- ◆ Collaboration
- ◆ Training



THANK YOU

