Endocrine Care in Fibrous Dysplasia and McCune Albright Syndrome

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- These pose no conflicts of interest for this presentation
- The opinions presented today are my own

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FOP patients and families
The IFOPA

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NIH National Institute of Diabetes and Digestive and Kidney Diseases

NIH National Center for Advancing Translational Sciences

NIAMS National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institutes of Health, Department of Health and Human Services

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RAISING MONEY FOR RARE DISEASE RESEARCH

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Department of Medicine
Institute for Human Genetics

REAC Junior Investigator Pilot Grant
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Today's Talk: Endocrine care in FD/MAS

- A hypothetical patient
- Brief discussion about endocrine considerations
  - Focusing on adult FD/MAS
- Questions and Answers

- For privacy and safety reasons, we can't address the individual medical concerns of any individual patient today. If you need medical assistance, please reach out to your physicians and medical team for advice.
- This presentation may discuss off-label or investigational therapies. You should discuss with your doctor whether these are appropriate before starting any of these therapies.
- Each patient is an individual and discussion/recommendations may or may not be appropriate for you. Discuss with your physician.

A hypothetical patient (sort of)

- 40 yo woman
- Former schoolteacher
  - Long history of pain
  - FD affecting left side of body, craniofacial
  - No known birthmarks
- Diagnosed with FD as a child
- Currently doing well, has a family, generally no concerns

Major ongoing concerns

- Over the past 10 years:
  - Chronic pain
  - Recently has felt that forehead and left cheek are getting more promnent

- Craniofacial FD
  - Changes in teeth, cavities, headaches

- Labs
  - Notable for normal calcium, phosphate
  - Elevated Alkaline Phosphatase (1000 range)

What has helped with management

- Originally diagnosed with FD
- Multidisciplinary care team
  - Ear, eye, endo, ortho, pain, dental
- Recognizing the balance of living life vs. the disease
  - Recognition that there may be a public face to the disease, but that background support is critical for the day to day.

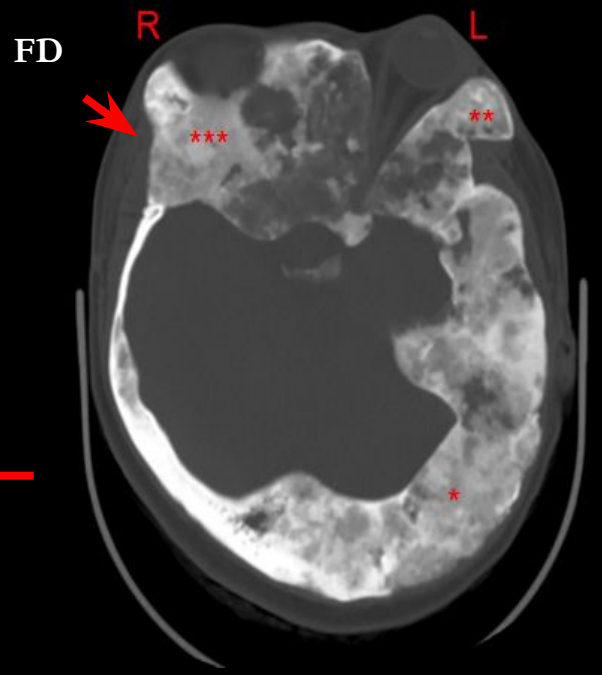
McCune-Albright Syndrome affects many organs

- **<u>Classical symptoms</u>**

- Café au lait skin lesions
- Fibrous dysplasia of the bone
- Endocrinopathies
  - Pituitary adenomas
  - Growth hormone / acromegaly
  - Early puberty / early periods
  - Thyroid hyperactivity / hyperthyroidism
  - Increased stress steroids / Cushing's syndrome
- Gastrointestinal growths
- Tooth fragility / Caries

Photo from NIH

Fibrous Dysplasia of the Bone can occur in MAS or as Mono-ostotic or Poly-ostotic Lesions



Lee et al, 2012

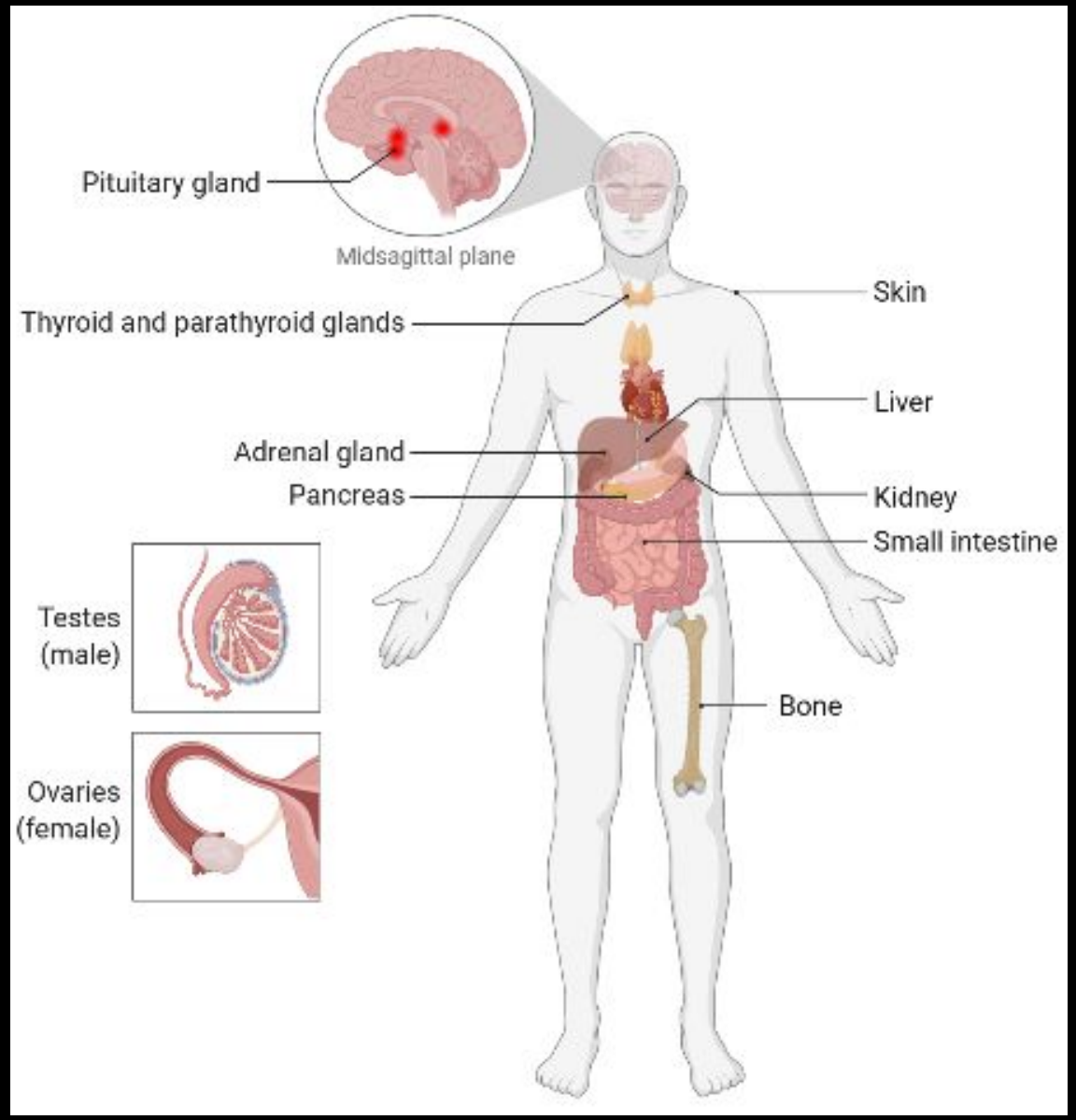
- Individual bones affected
- Can be mono-ostotic or poly-ostotic
- Every patient is an individual, and requires individual assessment and treatment

Photo: Brigham and Women's Hospital

Many Aspects of MAS Present Early in Life

- These are often definitively managed early on

- Growth hormone hypersecretion
  - Often pituitary hyperfunction, treat medically if needed.
  - May present later in life, may require medication/medical management
- Hyperthyroidism
  - May require thyroid hormone replacement after surgical removal
- Adrenal tumors / Cushing syndrome
  - May require life long steroid replacement
- Fibrous dysplasia of the bone
  - May involve pain management and orthopedic interventions
  - Treatment for fractures, deformities



Javid, et al. Best Practice Guidelines, OJRD 2019

FD bone regrowth in adults

- Typically FD lesions stabilize by the 3rd decade

- New growth of a previously stable lesion should trigger reevaluation
  - Screening for growth hormone/IGF1 levels (late presentation of MAS)

  - Screening for thyroid hormone levels

  - Imaging – to make sure something else isn't stimulating growth
    - Local infection
    - Conversion to malignancy – extremely rare but important to look for

Our patient:

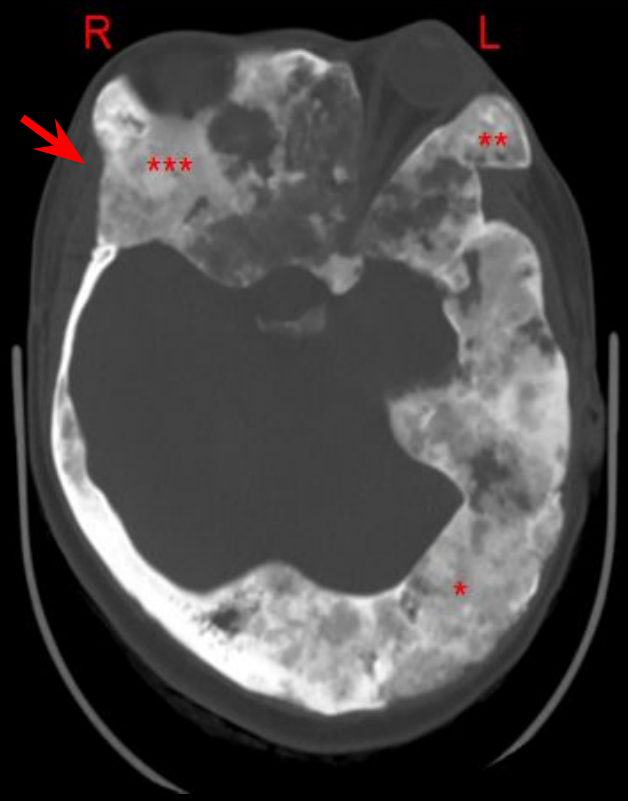
- IGF1 level was elevated to 170s
- Fasting growth hormone level also elevated
- Other hormones are OK

- CT imaging showed expansion of the FD lesion, no complications
- Patient was started on octreotide LAR
  - IGF1 came down to 112
  - Alk phos came down from 1300s -> 1100

- Continuing to try and optimize elevated AP level

Bone Health and Fibrous Dysplasia

- FD lesions tend to stabilize by the 3rd decade of life
  - Growth of a FD lesion should prompt evaluation for growth hormone hypersecretion, development of a bone tumor, or other type of complication
- Fractures can continue to occur as FD bone is weaker than normal
- Patients are still susceptible to other common conditions
  - Osteoporosis – may require denosumab or bisphosphonate
  - Arthritis (may be accelerated due to deformities)
- Hearing and vision screening should continue
- Dental health can also degrade, especially if bone lesions are in the jaw around the teeth
  - Poor integration with implants
  - Tooth fragility



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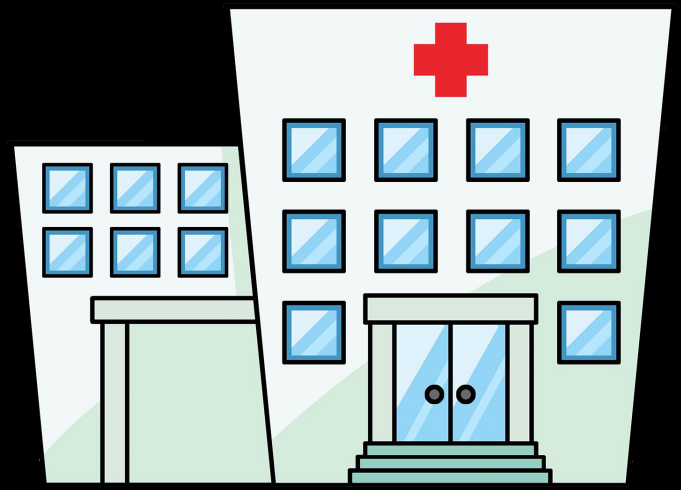
Changes in Women with FD/MAS

- Gynecologic changes are common in women with MAS
  - Irregular periods
  - Abnormal uterine bleeding
  - Infertility
  - Ovarian cysts
  - Primary ovarian insufficiency
- Spontaneous pregnancy is possible
- Change in FD related bone pain can occur
- No clear changes in bone or pregnancy outcome
- OCPs may help with control of symptoms

Boyce, et al. OJRD 2019

Look for December 2022 webinar on Fertility and FD/MAS
Dr. Gomez-Lobo from the NIH

Cancer Screening



- GNAS mutations are found in other types of cancers
  - Thyroid
  - Pancreas
  - Breast
- The gene is important for controlling cell replication
- FD/MAS may have higher a slightly higher risk of thyroid, cervical, breast, prostate, and melanoma cancers
- Potential for malignant transformation of FD lesions
  - Osteosarcoma, chondrosarcoma
- Age-appropriate cancer screening should be done, on time

M Hagelstein-Rotman, Calc. Tissue Int 2021; Majoor, IBMR 2018

MAS Patients: Endocrinology in Surgical Planning

- Important that any time a surgery is planned - involve the team!

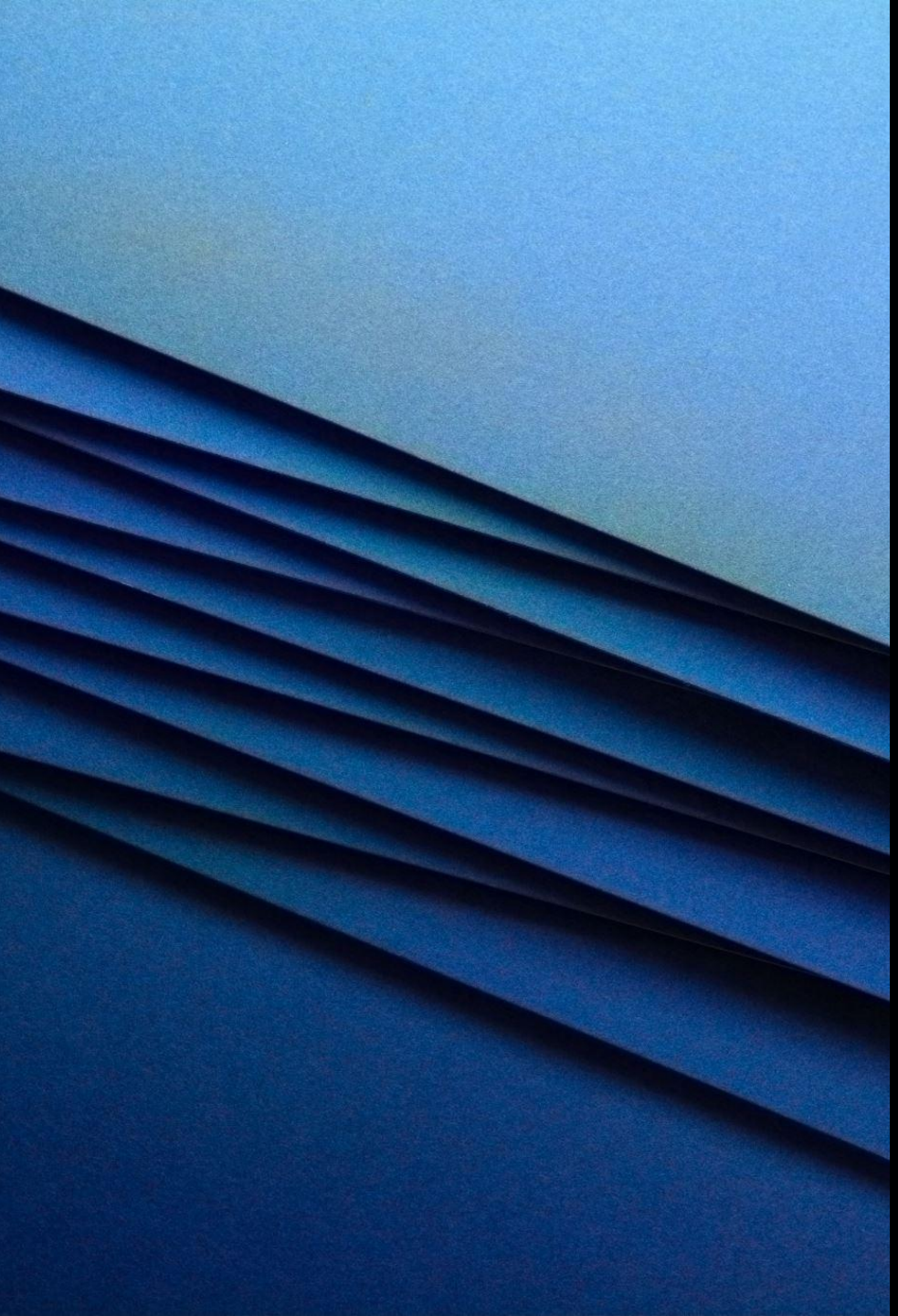
- Endocrinologist
  - Prior history of pituitary surgery
  - Prior history of sodium imbalance (ie on desmopressin)
  - Or on steroid replacement (ie after adrenal surgery)

  - Needs careful management of sodium and steroids in setting of surgery

Develop a Comprehensive Care Team

- Primary care physician
- Metabolic Bone Specialist (often Endocrinology or Rheumatology)
- Orthopedic Surgery
- Mental health specialist
- Nephrologist
- Pain management specialist
- Dentist
- Consider a palliative care team
- Home health team (if needed)

- For everyone: Important to discuss advance planning/estate planning with family, physicians, tax advisors, and estate planners



Key Considerations

Know	Each patient will have individual needs, depending on organs involved
Help	Your physician can help guide management
Screen	Make sure to do your regular cancer screening, on time
Give	Give the treatment guidelines to your doctors • FD/MAS Alliance website

Telehealth

Do

Do your visit from a quiet place – treat it like a regular doctor's visit

Check

Make sure your technology works

- Zoom or Hospital specific video applications
- Internet access/phone signal
- Your camera works

Don't

Please don't do it while driving

Optimizing Telehealth

- Convenient way for checkups, especially when no active issues

- Some assessments are best done in person
  - Physical exams – joint exams, thyroid exams, etc.
  - Bloodwork
  - X rays

- If you have hearing loss, telemedicine may not work as well
  - Have a companion on the call to make sure you catch everything

- Gather information together
- Have your medications list and pharmacy info ready
- Have a list of questions ready
- Be aware of laws governing interstate care
  - You may need a local physician to manage orders, prescriptions

Resources

- **Treatment guidelines:**
  - Javaid MK, et al. Best practice management guidelines for fibrous dysplasia/McCune-Albright syndrome: a consensus statement from the FD/MAS international consortium. Orphanet J Rare Dis. 2019 Jun 13;14(1):139. doi: 10.1186/s13023-019-1102-9. Erratum in: Orphanet J Rare Dis. 2019 Nov 21;14(1):267. PMID: 31196103; PMCID: PMC6567644.

- **FD/MAS Alliance:** FDMASalliance.org
  - FD/MAS Alliance provider directory

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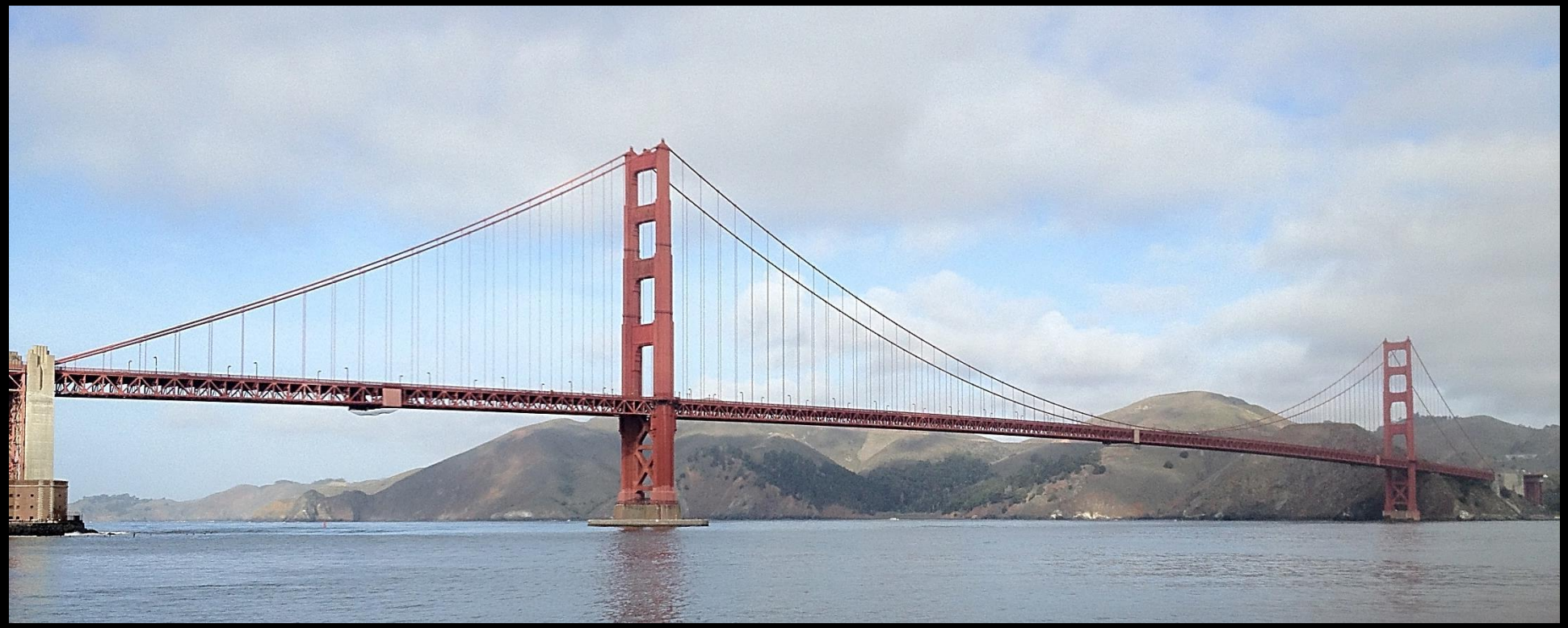

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