Harmful Algal Blooms Affects on Animals and Humans

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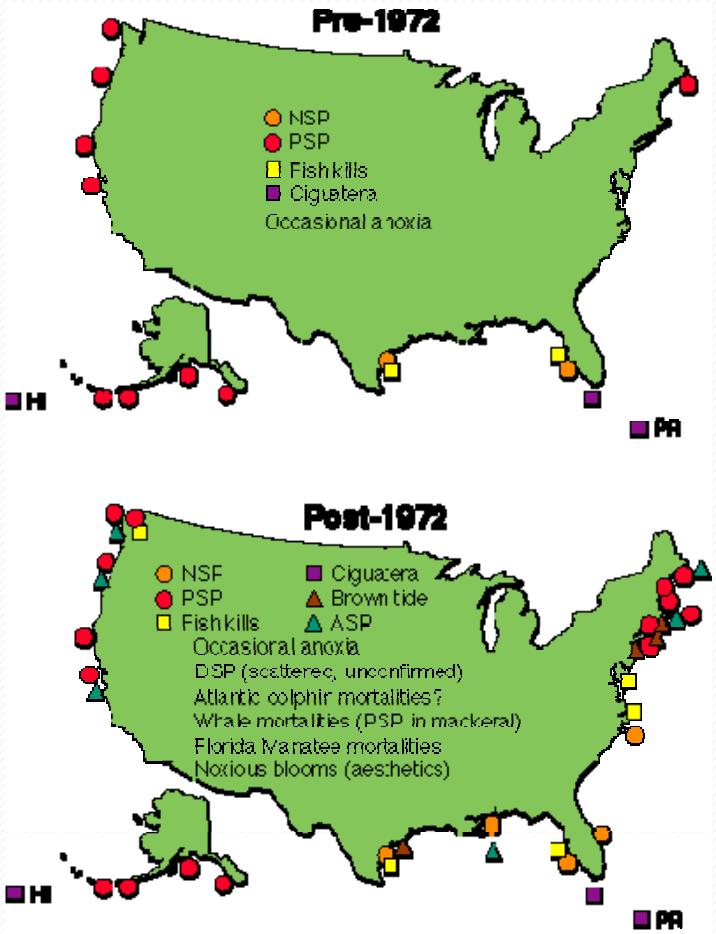
Harmful Algal Blooms

- Dinoflagellates
  - Saxitoxin (PSP)
  - Ciguatoxin (CFP)
  - Brevetoxin (NSP)
- Diatoms
  - Domoic Acid (ASP)

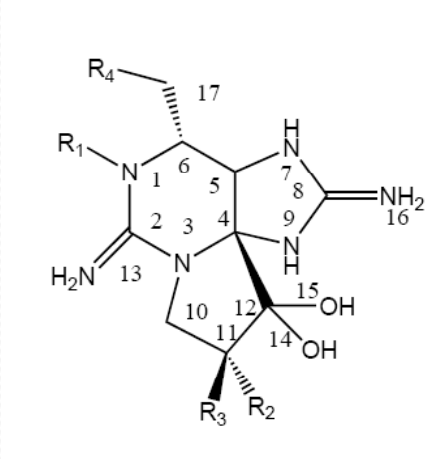


Source:
NOAA National Office for HABs

Saxitoxin

- Produced by *Alexandrium, Gymnodinium, Pyrodinium sp., cyanobacteria*
- Binds to receptor site 1 of voltage-gated sodium channels in cell membranes
- Blocks influx of Na; restricts signal transmission

- SF 1927, 100 ill, 6 deaths
- Ingestion of shellfish, snails or crustaceans
- Mouse LD50 = 10 µg/kg IP
- Human lethal dose 1-4 mg



Saxitoxin – Human Impacts

- Acute Clinical Signs
  - GI signs (V/D/N) 6-24 hrs
  - Neuro signs 1-2 days
    - Numbness/Tingling
    - Muscle weakness
    - Ataxia, incoordination
    - Resp. paralysis/death
      - (outbreaks up to 8% mortality)
- Diagnosis
  - Mouse bioassay
  - HPLC
  - Clinical signs, hx ingestion shellfish
- Treatment
  - Supportive care
    - IV Fluids
    - Activated charcoal

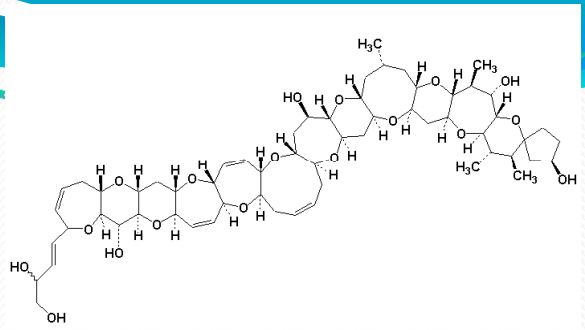
Saxitoxin – Animal Impacts

- Shellfish
- Crustaceans
- Pufferfish
- Fish kills – Herring, Mackerel
- Sub-lethal effects in fish larvae

Geraci et al 1989 J Fish Aq Sci;
Reyero et al 1999 Nat Toxin;
Landsberg 2002 Rev Fish Sci;
Samson et al 2008 J Fish Bio

- Strandings
  - Sea turtles
  - Sea birds
  - Humpback whales
  - Mediterranean monk seals

Ciguatoxin



- Produced by *Gambierdiscus sp.*
- Binds to receptor site 5 of voltage-gated sodium channels in cell membranes
- Causes neuronal & muscle cell depolarization
- Ingestion of reef fish in tropical/subtropical areas
  - Groupers, amberjack, red snappers, eel, sea bass, barracuda, and Spanish mackerel
  - Affects 10,000-50,000 people/yr
  - Mouse LD50 = 0.45 µg/kg IP

Ciguatoxin – Human Impacts

- Acute Clinical Signs
  - GI signs (V/D/N) 6-24 hrs
  - Cardiac signs 6-24 hrs
    - Hypotension/bradycardia
  - Neuro signs 1-2 days
    - Numbness/Tingling feet/hands/lips
    - Pruritis
    - Muscle pain
    - Reversal of hot/cold temp
- Chronic Signs
  - Weakness dys to wks
  - Neuro signs wks to mos
    - Numbness
    - Pruritis
    - Depression/fatigue
  - Diff Caribbean/Pac
    - Caribbean GI signs
    - Pac Neuro signs

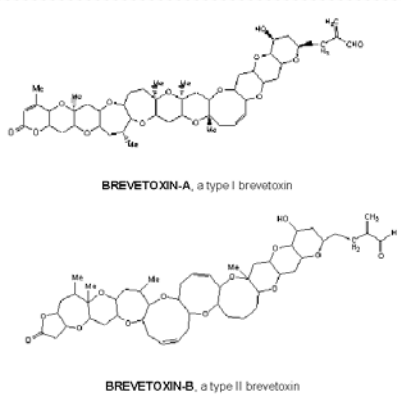
Friedman et al 2008 Marine Drugs

Ciguatoxin – Human Impacts

- Diagnosis
  - No test available
    - Can test tissues of ingested fish
  - Clinical signs, history of ingestion reef fish
- DDX
  - Brevetoxin, scombroid/pufferfish toxicity, botulism, OP toxicity
- Fish testing (FDA)
  - In vitro mouse neuroblastoma assay
    - Differentiates between CTX, PbTx & STX, TTX
  - LC-MS
- Treatment
  - Mannitol 0.5-1.0 g/kg IV over 30-45 mins
  - Supportive care

Brevetoxin

- Produced by *Karenia sp.*
- Binds to receptor site 5 of voltage-gated sodium channels in cell membranes
- Causes neuronal & muscle cell depolarization
- Ingestion of shellfish or inhalation of aerosols
- Mouse LD50 = 170 µg/kg IP
- Metabolized by liver & kidney
- Action limit 20MU/100g



Brevetoxin – Human Impacts

- Acute Clinical Signs (Ingestion)
  - GI signs (V/D/N) 6-24 hrs
  - Neuro signs 24 hrs
    - Numbness/Tingling
    - Reversal of hot/cold temp
    - Incoordination
    - Ataxia
- Diagnosis
  - Mouse bioassay
  - Elisa/LC-MS
    - Urine/Feces /Blood
    - Ingested food
  - Clinical signs, history of ingestion shellfish
- Treatment
  - Supportive care
  - +/- Mannitol

Watkins et al 2008 Marine Drugs

Brevetoxin – Human Impacts

- Acute Clinical Signs (Inhalation)
  - Respiratory signs
    - Throat irritation
    - Sneezing, coughing
    - Itchy, watery eyes
  - Asthmatics & COPD indiv. more susceptible, decreased pulmonary function

Abraham et al 2005 Env Hlth Persp;
Fleming et al 2007 Chest

- Diagnosis
  - Red tide bloom offshore, winds onshore
- Treatment
  - Removal from area
  - Albuterol (asthmatics)

Source: B. Kirkpatrick

Brevetoxin – Animal Impacts

- FISH
  - Skin/gill exposure; acute mortality
  - Ingestion
    - No effects to mortality
  - Secondary hypoxia/anoxia

- Highest levels in planktivorous fish
- Highest levels of toxin in liver, stomach contents
- Elimination ½ life of 24 days for menhaden tissues after oral exposure

Naar et al 2007 Toxicon;
Hinton & Ramsdell 2008 Mar Eco Prog Ser

Brevetoxin – Animal Impacts

- MANATEES – FL
  - 1982, 1996, 2002, 2005 (n=308 deaths)
  - Toxin - ingestion, inhalation
- Clinical signs
  - Increased Respiration
  - Tremors/Lip twitching
  - Listing/unable to stay dorsal

Bossart et al 1996 Tox Path
Flewelling et al 2005 Nature

- Treatment
  - Remove from area (if inhalation)
  - Supportive care

Brevetoxin – Animal Impacts

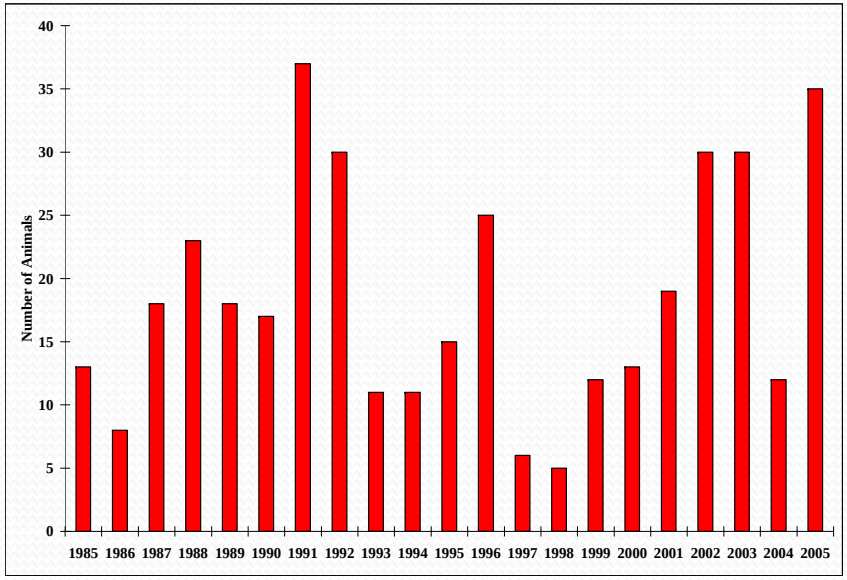
- DOLPHINS – West FL
  - 1996, 1999, 2002-2005
  - Toxin - ingestion
  - Acute mortalities
  - No live strandings
    - Low Brevetoxin levels in gastric, urine, feces from live free-ranging dolphins

Flewelling et al 2005 Nature;
Fire et al 2007 Mar Bio
Fire et al 2008 Mar Mam Sci

- Panhandle FL 2004
  - 107 dead dolphins
  - 4 wk period
  - Menhaden in stomachs
    - >10-20 ,000 ng/g in fish
    - 1-10,000 ng/g in dolphin tissues

Brevetoxin – Animal Impacts

Mote Yearly Dolphin Strandings



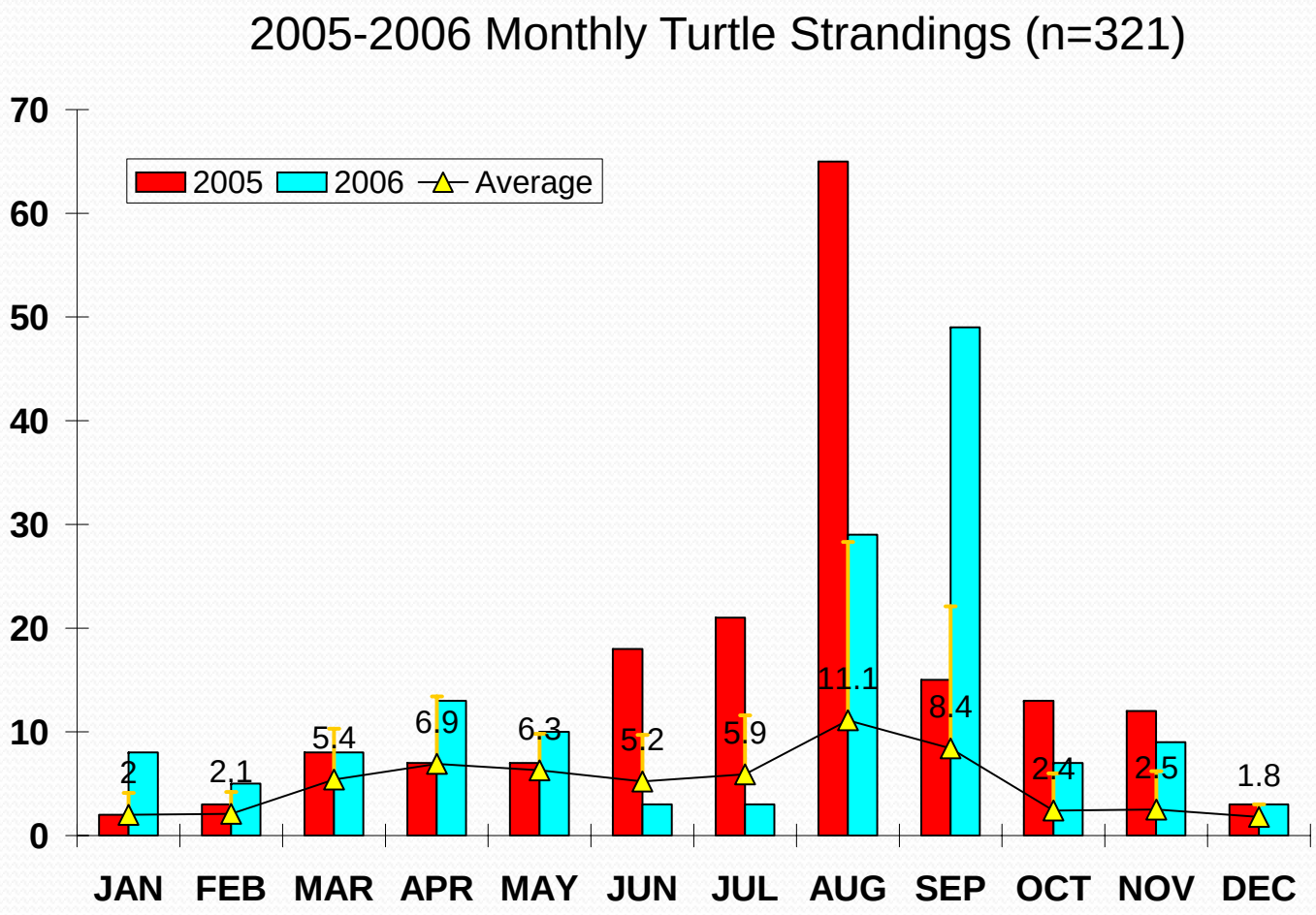
2005 Dolphin Brevetoxin
Tissue Levels (ng/g; n=20)

Dolphins	Liver	Stm Cnts	Feces
N	20.0	19.0	16.0
Mean	31.3	291.3	1260.8
ST Dev	29.6	580.6	2930.8
Median	19.3	67.8	53.5
Range	5-124.0	5-2141.0	5-11226.0

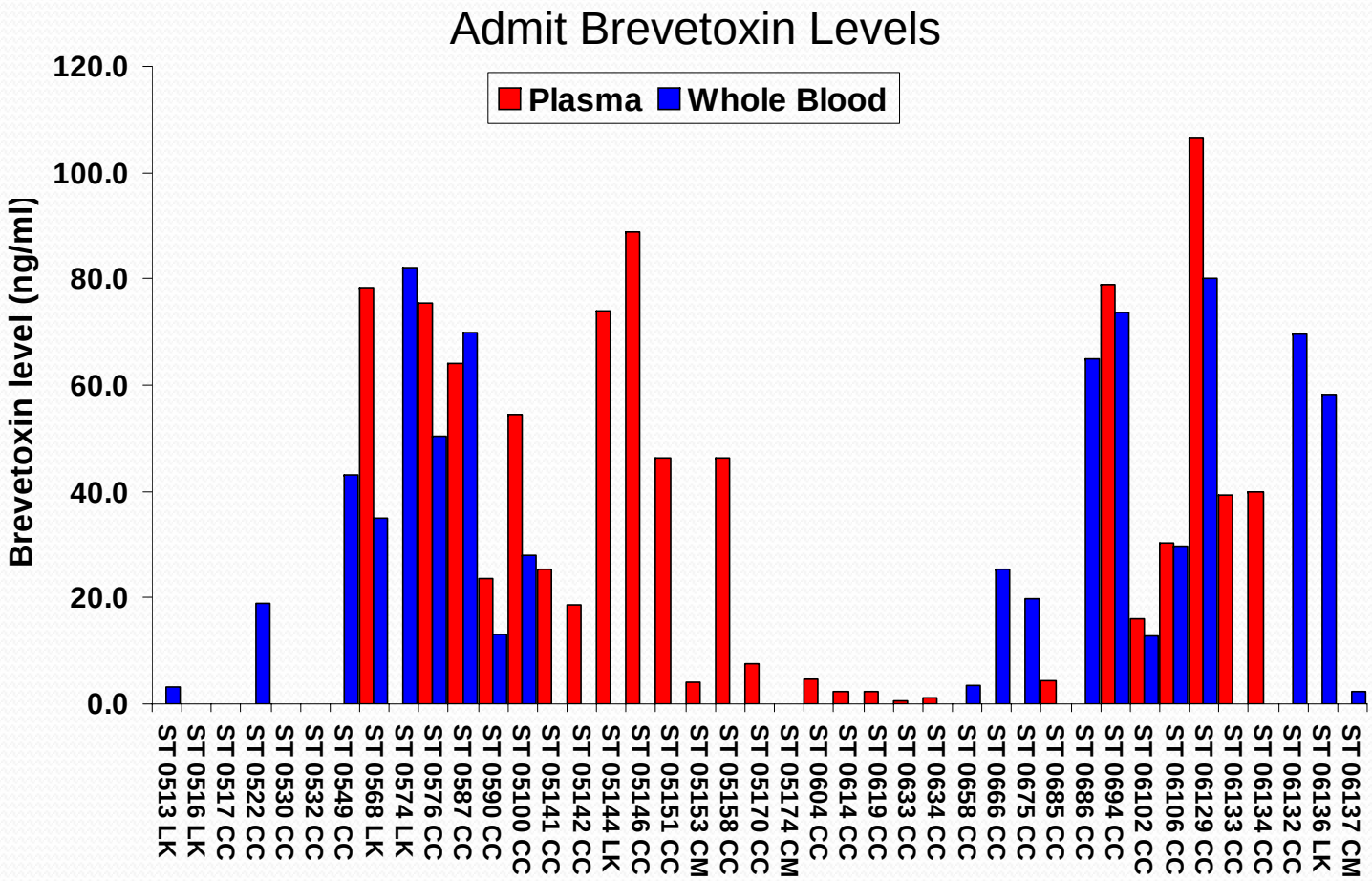
Brevetoxin – Animal Impacts

- SEA TURTLES – West FL
  - 1996, 2005, 2006
  - Toxin – ingestion, inhalation
- Clinical signs
  - Unresponsive, circling, twitching
  - Comatose – (Loggerheads)
  - Swollen eyes
  - Good body weight
- Treatment
  - Supportive Care
  - Lasix 5 mg/kg SID 1-3 dys
  - +/- Benadryl

Brevetoxin – Sea Turtles

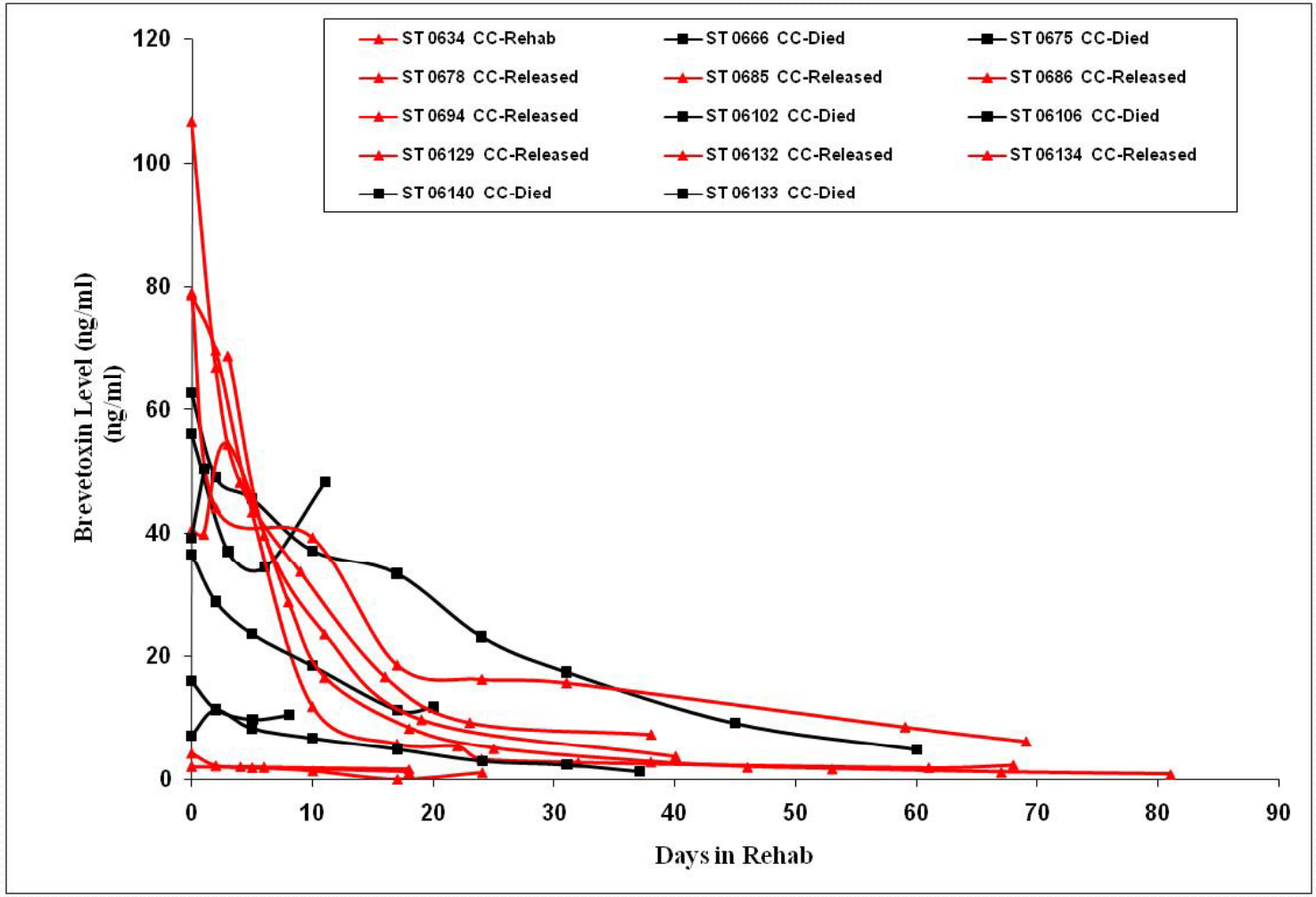


Brevetoxin – Sea Turtles



Brevetoxin – Sea Turtles

Clearance of brevetoxin from plasma (n=14)



Brevetoxin – Animal Impacts

- SEA BIRDS
  - 1996, 1997-99, 2005
  - Toxin – ingestion, inhalation
- Clinical signs
  - Inability to stand
  - Ataxia, incoordination
  - Seizures
- Treatment
  - Supportive care
  - Anti-convulsants

Kreuder et al 2002 J Zoo Wild Med

Brevetoxin Tissue Levels

Sea Turtle (n=26)

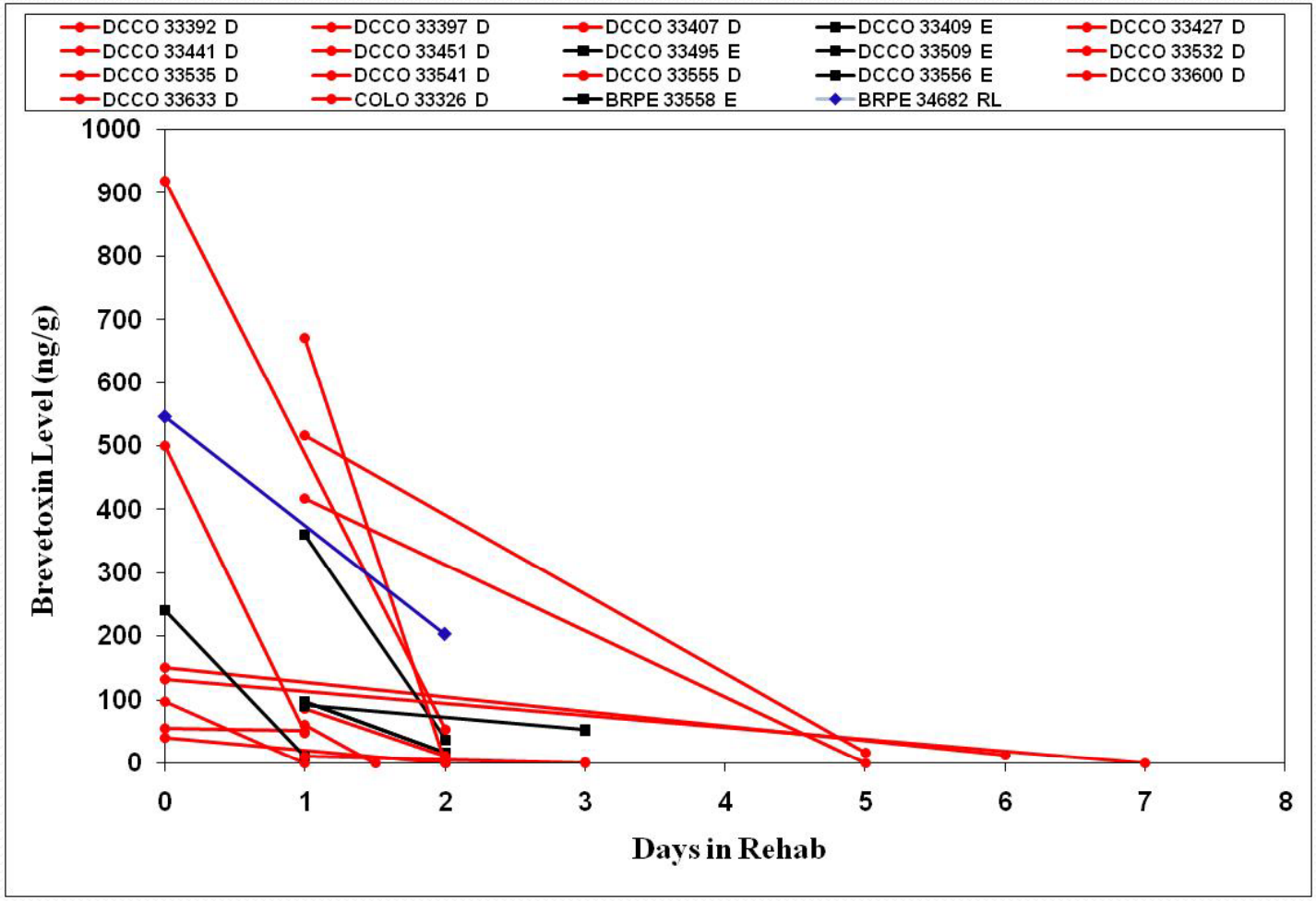
Tissue	Lung	Liver	Kidney	St Cnts	Feces	Bile	Urine	SI Fluid	LI Fluid	Admit Blood
Mean	129.70	77.03	40.68	1916.21	208.73	64.99	81.34	256.27	746.31	24.91
St Dev	49.93	116.81	37.48	3815.18	439.96	103.41	242.93	567.81	986.97	26.56
Count	2	26	16	9	18	19	12	13	2	13

Sea Bird (n=21)

Tissue	Liver	Kidney	Lung	Brain	Feces	St Cnts	Bile	Feces Live
Mean	39.82	27.92	11.68	21.43	33.80	68.02	291.75	260.24
St Dev	28.32	16.84	8.76	28.23	29.38	81.76	328.14	256.40
N	30	21	12	18	21	9	3	18

Brevetoxin – Sea Birds

Clearance of brevetoxin from feces (n=15)

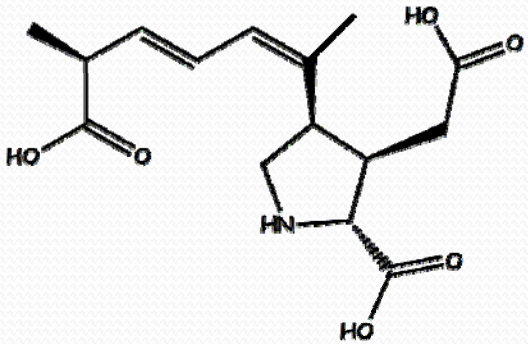


Brevetoxin – Ecological Impacts

- 63% (n=74) of dolphins in 2002-2006
- 64% (n=78) of sea birds 2005-2006
- 95% (n=99) of sea turtles 2005-2007
  - Positive for brevetoxin in blood, feces or at least one tissue at necropsy
- Brevetoxin, may play a greater role in regulating populations by negatively impacting individual health and decreasing survival

Domoic Acid

- Produced by *Pseudonitzschia sp.*
- Binds to glutamate receptors on neurons in the CA3, CA4 regions of the hippocampus
- Causes neuronal excitation and seizures
- First identified when about 100 humans were poisoned, 3 died, in eastern Canada in 1987
- ½ life 4 hrs rat plasma



Domoic Acid – Human Impacts

- Acute Clinical Signs
  - GI signs (V/D/N) 24 hrs
  - Neuro signs 24-48 hrs
    - Weakness
    - Memory loss
    - Seizures
    - Coma
  - Cardiac signs
    - Hyper/hypotension
    - Arrhythmias
- Diagnosis
  - Mouse bioassay
  - HPLC – feces/urine
  - Testing ingested food
  - Clinical signs, history of ingestion shellfish
- Treatment
  - Supportive
  - Anticonvulsants

Domoic Acid – Animal Impacts

- Invertebrates
  - Clams, Oysters, Mussels
  - Peanut Worm, Ghost Shrimp, Hermit Crab
  - Sand & Dungeness Crabs
  - Krill
    - Reduced grazing rates
- Fish
  - Sanddabs, Mackerel, Albacore
  - Anchovies/sardines
    - No effect GI absorption
    - Neuro effects IP

Bargu et al 2006 Mar Eco Prog Ser;
Bejarano et al 2008 Hum & Eco Risk Assess;
Kivek et al 2008 Mar Eco Prog Ser

Lefebvre et al 2001 Mar Bio;
Lefebvre et al 2002 Toxicon

Domoic Acid – Animal Impacts

- Sea Bird Strandings
  - Santa Cruz, 1991
  - Brown pelicans, Brandt's cormorants
    - Disorientation
    - Incoordination
    - Seizures
    - Headweaving, scratching
  - Additional outbreaks 2002, 2006

Source: IBRRC

Work et al 1993 J Zoo Wild Med;
Sierra-Beltran et al 1997 Toxicon

Domoic Acid – Animal Impacts

- Sea otter Strandings
  - Myocarditis/dilated cardiomyopathy (n=6)

Kreuder et al 2005 Am J Vet Res

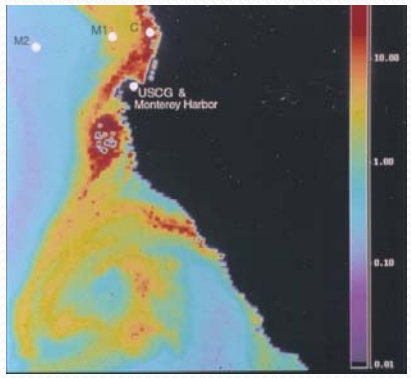
- Cetacean Strandings - 2002
  - Long-beaked common dolphins
  - Short-beaked common dolphins
  - Grey/humpback/blue whales

Heyning 2003 NOAA Tech Mem

Domoic Acid – Animal Impacts

- California Sea Lion Strandings
- First identified in marine mammals in 1998
- 70 sea lions stranded in Monterey Bay, 400 others died along the California coast
- Animals had altered behavior and severe seizures
- Neuronal necrosis in the hippocampus

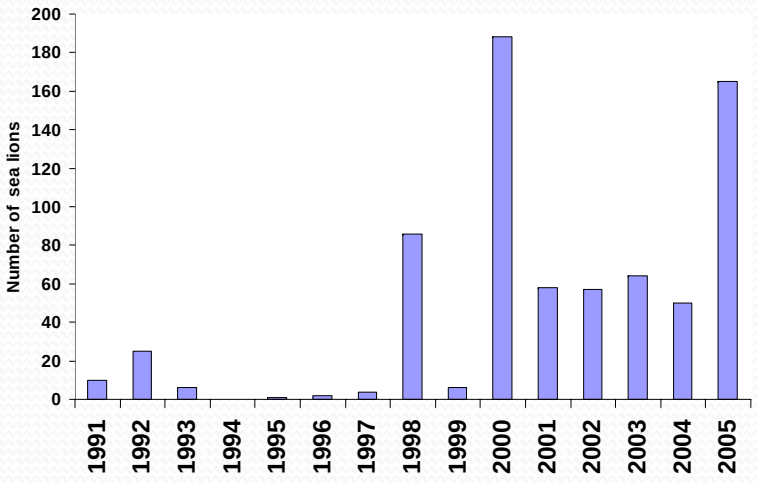
Scholin et al 2000 Nature



Domoic Acid – Sea Lions

- Temporal and spatial association among bloom, DA in diatoms, DA in prey, DA in sea lions, clinical signs and strandings
- Detected in sea lions before high levels were detected in mussels
- Sea lions a good sentinel of DA blooms

HAB Associated California Sea Lion Strandings



Domoic Acid – Sea Lions

- Acute Clinical Signs
  - Seizures
  - Ataxia/head weaving
- Treatment
  - Supportive care
  - Lorazepam 0.1 mg/kg IM
  - Phenobarbital 4mg/kg IM 2 days; 2mg/kg IM 5 days

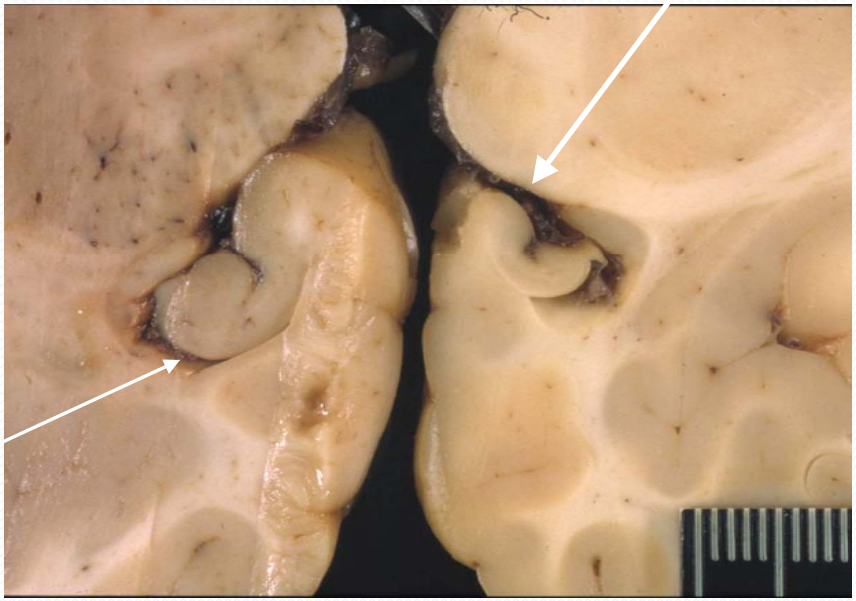
Gulland et al 2002 Vet Record

- Chronic Clinical Signs
  - Stranding with seizures DA bloom absent
  - Epileptic seizures
  - Abnormal behavior
    - Aggression, abnormal stranding locations

Domoic Acid – Sea Lions

- Pathology
  - Neuronal atrophy, loss, and gliosis
  - Uni- or Bilateral hippocampal atrophy

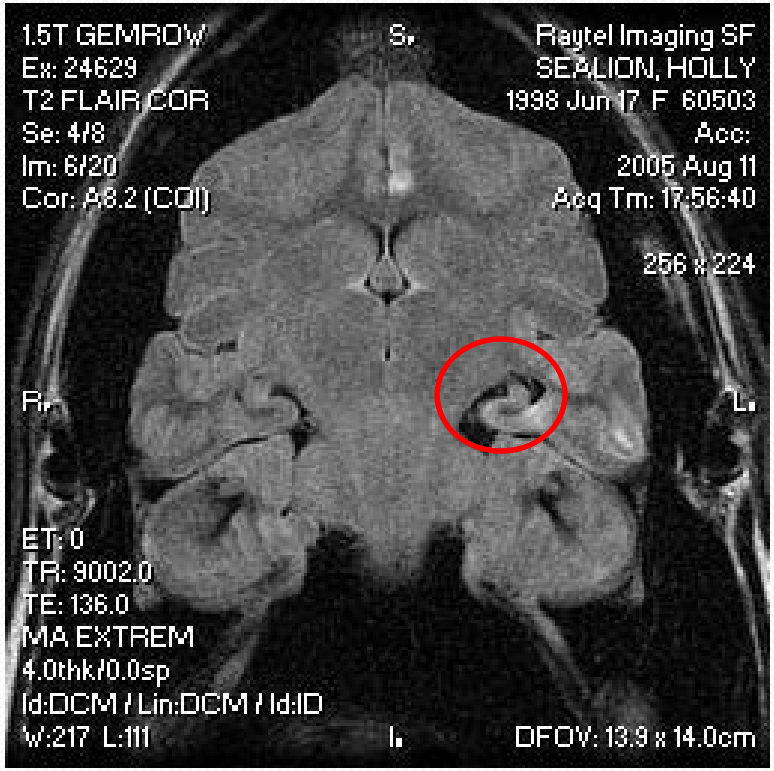
Hippocampal atrophy



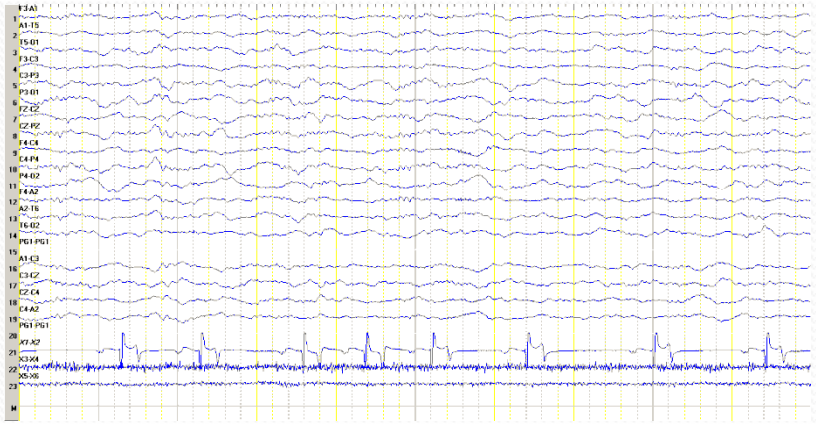
Normal hippocampus

Silvagni et al 2005 Vet Path

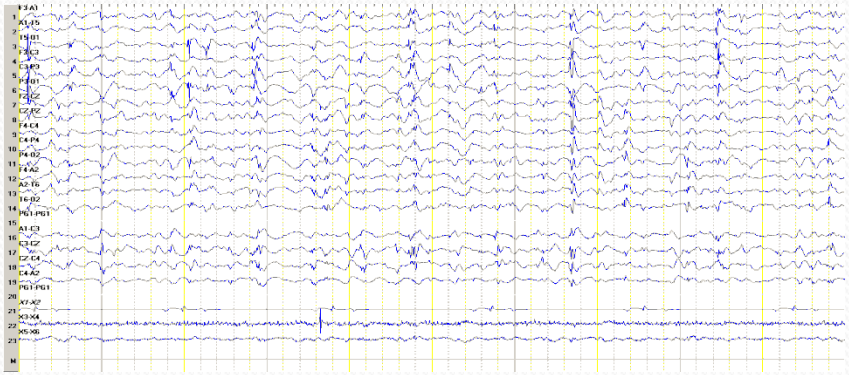
Domoic Acid – Sea Lions



Unilateral hippocampal atrophy and temporal horn enlargement



Normal



Epileptiform pattern

Goldstein et al 2007 Proc Roy Soc B

Domoic Acid – Sea Lions

- Reproductive Effects
  - 168 females stranded with neurological signs in 2002-2004 had reproductive failure
  - 101 abortions, 31 premature live births
  - 36 dead in utero pups
  - Serology, culture and histopathology ruled out infectious causes

Brodie et al 2006. Marine Mammal Science

Domoic Acid – Sea Lions

- Domoic acid detected in fetal urine 8 days after adult female stranded (exposed)

	Maternal Urine	Fetal Feces	Fetal Urine	Fetal Gastric Fluid	Amniotic Fluid
RBA	6/6	1/1	6/6	17/25	24/40
LC-MS	5/5	0/0	4/6	8/8	16/20

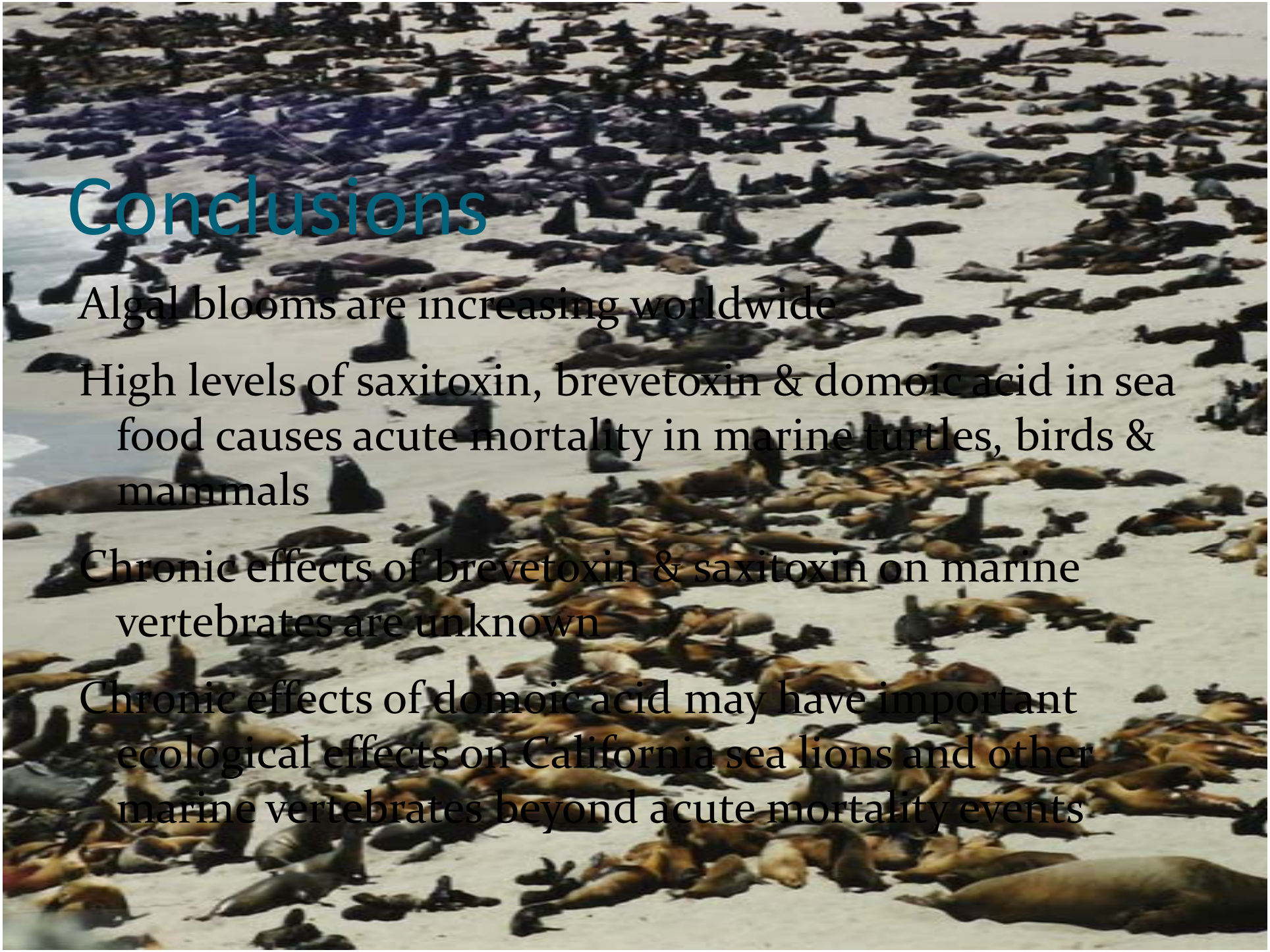
- Domoic acid crosses the placenta
- Domoic acid accumulates in amniotic fluid - “sink”
- Fetal death, abortion and premature parturition observed – anoxia or direct toxicity?

Maucher and Ramsdell 2007 Env Hlth Persp

Domoic Acid–Ecological Impacts

- Sea Lions
  - Acute mortality
  - Subclinical seizures
  - Epilepsy
  - Neuronal loss and hippocampal atrophy
  - Abortion
  - Premature parturition
- Mainly affects adult females
  - 200,000 sea lions
  - Pop decrease in adult females
  - Loss of fetus/pups
  - Overtime may lead to decrease in pop growth

Bejarano et al 2008 Mar Mam Sci



Conclusions

Algal blooms are increasing worldwide

High levels of saxitoxin, brevetoxin & domoic acid in sea food causes acute mortality in marine turtles, birds & mammals

Chronic effects of brevetoxin & saxitoxin on marine vertebrates are unknown

Chronic effects of domoic acid may have important ecological effects on California sea lions and other marine vertebrates beyond acute mortality events

Funding for Brevetoxin & Domoic Acid Studies

EPA Star Fellowship

Morris Animal Foundation

NMFS Prescott Grant Program

NOAA Oceans and Human Health Initiative

Protect Wild Dolphins License Plate

Sea Turtle License Plate