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CLINICAL AND PATHOLOGICAL CHARACTERIZATION OF NORTHERN ELEPHANT SEAL SKIN DISEASE

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ABSTRACT: From 1984 through 1992, staff at The Marine Mammal Center (TMMC, Sausalito, California, USA) examined 207 northern elephant seals (*Mirounga angustirostris*) with a condition of unknown etiology called northern elephant seal skin disease (NESSD). The skin lesions were characterized by patchy to extensive alopecia and hyperpigmentation, punctate or coalescing epidermal ulceration, and occasionally, massive skin necrosis. Microscopic lesions included ulcerative dermatitis with hyperkeratosis, squamous metaplasia and atrophy of sebaceous glands. All diseased seals were less than 2 years of age and suffered from emaciation, depression, and dehydration. Mortality from septicemia increased significantly with severity of skin ulceration. Compared to 14 apparently unaffected seals, diseased seals had depressed levels of circulating thyroxine, triiodothyronine, retinol, serum iron, albumin, calcium, and cholesterol. Levels of alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, gamma glutamyl transpeptidase, blood urea nitrogen, and uric acid were elevated. Morphometrically, diseased animals were approximately 15% smaller than normal seals of the same age. Serum and blubber concentrations of 36 polychlorinated biphenyl congeners (ΣPCB) and dichloro-diphenyl-dichloroethylene (p,p'-DDE) were negatively correlated with body mass. Mean concentrations of ΣPCB and p,p'-DDE in serum in diseased seals were elevated as compared to apparently normal seals. Etiology of this syndrome remains unknown, but the possibility of PCB toxicosis cannot be ruled out.

Key words: Northern elephant seal, *Mirounga angustirostris*, hyperkeratosis, squamous metaplasia, ulcerative dermatitis, skin disease, PCB, DDT.

INTRODUCTION

Several skin diseases have been recognized in pinnipeds, primarily of infectious etiology. Viral infections have included pox (Wilson et al., 1969) and caliciviruses (Smith and Akers, 1973). Bacterial conditions have included dermatophilosis (Frese and Weber, 1971), streptococcosis (Eriksen, 1962), mycobacteriosis (Wells et al., 1990), staphylococcosis (Wilson and Long, 1970), and others (Anderson et al., 1974; Rand, 1975). Parasitic diseases have included pediculosis, demodecosis (Sweeney, 1986), and sarcoptic mange (Sweeney, 1974). Fungal conditions have included dermatophytosis, candidiasis (Lauckner, 1985) and *Fusarium* spp. mycosis (Montali et al., 1981; Frasca et al., 1996). Hypovitaminosis A dermatosis (Wallach and Boever, 1983) and hypovitaminosis E associated aberrant molt (Engelhardt and Geraci, 1978) are the only nutritional skin diseases that have been documented in pinnipeds. An ulcerative dermatitis has been observed in grey seals (*Halichoerus grypus*) from the Baltic Sea which may be associated with PCBs and related chemicals (Bergman and Olsson, 1985).

Northern elephant seal skin disease (NESSD) is a potentially fatal condition afflicting immature northern elephant seals (*Mirounga angustirostris*) (Gerber et al., 1993). Since 1975, staff of The Marine Mammal Center (TMMC, Sausalito California, USA) have recognized NESSD as a specific syndrome in stranded northern elephant seals characterized by generalized, ulcerative dermatitis (Figs. 1 and 2).

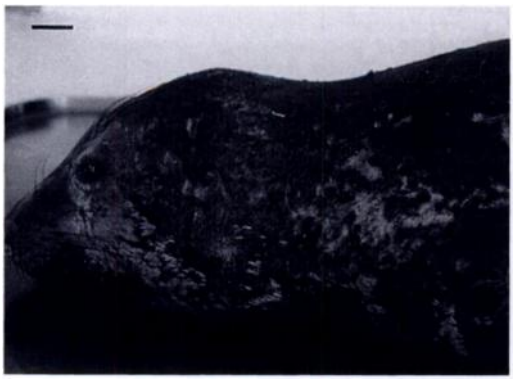

FIGURE 1. Gross appearance of a stranded female juvenile *Mirounga angustirostris* with severe lesions of northern elephant seal skin disease. Bar = 25 cm.

FIGURE 2. Close up of skin lesions from seal in Figure 1. Bar = 6.8 mm.

Although considered to be an important skin disease of pinnipeds (Bossart and Dierauf, 1990), the syndrome has been poorly documented and is of unknown etiology.

While only juveniles, 9 mo to 2 yr, have been treated for the condition at TMMC, affected subadult northern elephant seals occasionally have been observed in the wild. Adult cases of the disease are extremely rare; only three possible cases were observed between 1986 and 1991 at the Año Nuevo California State Reserve rookery (P. Morris, pers. comm.), where researchers have referred to the condition as scabby molt (LeBoeuf and Laws, 1994).

Like the northern elephant seal, both the Hawaiian monk seal (*Monachus schauinslandi*) and the southern elephant seal (*Mirounga leonina*) undergo an annual catastrophic skin molt (Ling, 1978). The seals fast while their epidermis is shed along with the pelage. No skin disease similar to NESSD has been reported in either of those species. Carrick and Ingham (1962) referred to skin lesions of an unknown etiology in a southern elephant seal but the photographs did not appear to be consistent with the gross appearance of NESSD.

A retrospective study of pre-existing 8 yr of medical records and a prospective study of a cohort of northern elephant seals was undertaken in 1992 to characterize NESSD. In this report, we present an analysis of the seasonal, clinical pathological and histopathological alterations associated with NESSD. In conjunction, dichloro-diphenyl-trichloroethane and metabolites (DDTs) and polychlorinated biphenyl (PCBs) levels were analyzed in diseased and clinically normal animals to determine whether levels were correlated with disease status.

MATERIALS AND METHODS

Medical records were reviewed for 207 live stranded northern elephant seals treated at TMMC for skin diseases from 1984 to 1992. Necropsy records from 16 cases were also examined.

Gross skin lesions were classified by severity based on past experience. Mild cases were defined as possessing small (less than 2 cm in diameter) superficial excoriations or ulcerative lesions over less than half the body surface and patchy alopecia. Moderate cases had ulcers greater than 2 cm in diameter or lesions covering more than half the body surface and ex-

tensive alopecia with some degree of pigmentation, or thickening of the epidermis. Severe cases had large coalescing ulcers greater than 3 cm in diameter, which exuded blood, serosanguinous or purulent fluid, occasionally with necrosis of the underlying blubber layer.

Between February and May 1992, skin, blood, and blubber samples were collected under manual restraint from 15 yearling northern elephant seals with gross lesions of NESSD brought to TMMC. The severity of skin lesions were as follows: four mild cases (three female, one male); four moderate cases (three female, one male); and seven severe cases (five female, two male). Age assessment was based on behavior, body size, head shape, dentition, as well as tag number for nine individuals tagged as pups (D. Crocker, pers. comm.). Sex was determined by visual examination for a preputial or vaginal opening. Body weights were recorded. Similar skin, blood and blubber samples were collected from 14 clinically normal seals with no external indications of NESSD, that had hauled out to molt from April to June at the Año Nuevo State Reserve rookery (37°8′N122°20′W), California (USA). Animals were selected randomly from those accessible on the periphery of the rookery to minimize disturbance and for safety considerations. The group of normal yearling seals consisted of five females and three males in early molt, and four females and two males in late molt. Field sample collections were performed on seals that were sedated with Telazol® (Aveco Co. Inc., Fort Dodge, Iowa, USA) administered intramuscularly at a mean dosage of 0.9 mg/kg (range of 0.8–1.4 mg/kg). Sedation was maintained with intermittent doses of intravenous ketamine HCl (Ketaset®, Aveco Co. Inc.) at 1 to 2 mg/kg and diazepam HCl (Abbott Laboratories, North Chicago Illinois, USA) at 0.03 to 0.1 mg/kg.

Blood was collected from 1992 study animals from the extradural sinus into Vacutainer® (Becton Dickinson and Company, Rutherford, New Jersey, USA) tubes for hemograms, serum biochemistry and organochlorine level determination. Each seal had three blubber samples, approximately 100 mg each, taken through a single incision using sterile surgical technique, for contaminant analysis as described by Newman et al. (1994). All normal seals were released on the beach after full recovery from sedation or after being held in the laboratory for less than 12 hr.

Skin samples for aerobic culture were collected by rubbing the skin with swabs (Aerobic Starswab, Starplex Scientific, Etobicoke, Ontario, Canada) of 14 normal animals near the dorsal midline and 15 NESSD animals in lesions (one sample from a normal animal was lost during shipment). Swabs were held less than 24 hr in standard transport media and cultured at 37 C on 5% sheep blood and MacConkey agars (PML, Tualatin, Oregon, USA). In addition, anaerobic swabs (Anaerobic Culturette, Becton Dickinson and Company, Cockeysville, Maryland, USA) were obtained from skin of three normal and three NESSD animals and cultured anaerobically. Isolates were identified to genus and species by the criteria of Carter (1984). Identification of the Enterobacteriaceae was established using API® Strips (Analytab Products Division of Sherwood Medical, Plainview, New York, USA).

Skin biopsies were collected from 10 NESSD seals and three normal seals in early stages of molt with sterile 6 mm disposable Baker's® biopsy punches (Baker Cummins Pharmaceuticals, Miami, Florida, USA) as described by Muller et al. (1989). One biopsy from normal skin over the gluteal area was taken from normal animals, three were taken from each of 10 diseased seals, one from an early (not grossly necrotic) lesion, one from an area of alopecia, and one from grossly unaffected skin. Biopsy sites were flushed with a nitrofurazone solution and permitted to heal by second intention. One-half of one skin biopsy from each individual was used to inoculate Sabouraud dextrose agar (PML, Tualatin, Oregon) and incubated at 22 C for the isolation of fungi, the other halves were fixed in neutral-buffered 10% formalin. Formalin-fixed skin samples were embedded in paraffin, sectioned at 6 μm, and stained with hematoxylin and eosin.

Hematology and serum biochemical analyses of samples from the 15 NESSD and 14 clinically normal seals were performed by Marin Medical Laboratories (Greenbrae, California). Hematology and serum biochemistry results from 15 additional skin-diseased animals examined at TMMC the same year were also available and included for analysis. Serum vitamin A (retinol) levels were determined by high performance liquid chromatography (Smith-Kline Beecham Laboratory, Van Nuys, California) using a Perkin-Elmer LC25 detector (Perkin-Elmer, Norwalk, Connecticut, USA). Thyroxine (total T4) was measured by microparticle enzyme immunoassay, Abbott IMX® (Abbott Diagnostic Division, Irving, Texas, USA). Triiodothyronine (total T3) was measured by fluorescence polarization immunoassay using the Abbot IMX® system (Abbott Diagnostic Division). Electrolytes were determined on a Beckman CX3® (Diagnostic Industries, Beckman Instruments, Brea, California). The calcium values were determined

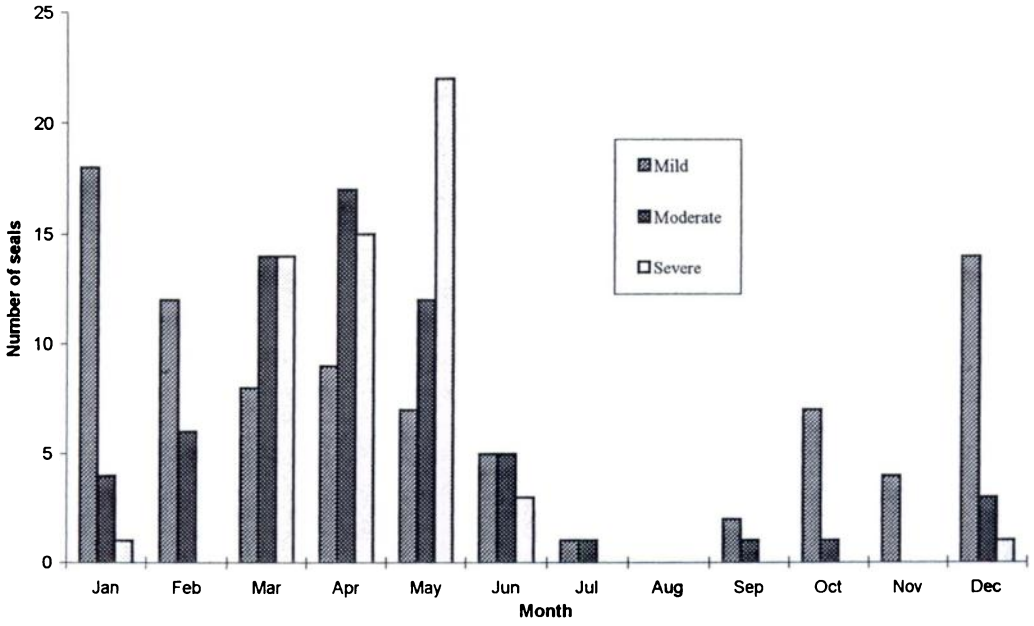

FIGURE 3. Monthly distribution of 207 northern elephants seals brought to The Marine Mammal Center, Sausalito, California, by severity of lesions of northern elephant seals skin disease from 1984 to 1992.

on a Beckman CX3® by Arsenazo III, Bichromic End-Point® (Diagnostic Industries, Beckman Instruments). The remainder of the serum chemistry values were determined on a Coulter DACOS Analyzer® with continuous optical scanning (Coulter Diagnostics, Hialeah, Florida). Complete blood cell counts were performed on a Coulter Counter ZBI® or Coulter S-Plus IV® (Coulter Diagnostics). Differential cell counts were performed manually at TMMC.

Matched serum and blubber biopsies from 14 normal and 10 diseased seals were analyzed for lipid content and organochlorine contaminants as described by Newman et al. (1994). The p,p′- and o,p′-chlorination isomers of DDT and their metabolites dichloro-diphenyl-dichloroethylene (DDE), and dichloro-diphenyl-dichloroethane (DDD) were quantified. Results were summed and reported on a lipid weight basis as ΣDDT. The PCB levels were sums of the 39 PCB congeners with two to nine chlorines per molecule (listed in Newman et al., 1994) and are reported on a lipid weight basis as ΣPCB.

Sites of morphometric measurements in 14 normal and 10 diseased seals were adapted from Gales and Burton (1987). Standard straight length, circumference at the ears and tarsus in cm were used to assess structural variability within the study groups. Due to the sexual dimorphism, the morphometric analysis was separated by sex.

Statistical significance was taken at P value <0.01 and marginal significance at $P < 0.05$. Data were analyzed for normalcy using the software package Statview II (Abacus Concepts Inc., Berkeley, California); blood and serum parameters were compared using the Student's t-test; morphometric measurements were compared using a Kruskal-Wallis H-test; blubber and serum ΣDDT and ΣPCB levels were compared using a Mann-Whitney U-test. Correlations between morphometrics and contaminants were made by a Spearman's rank correlation using Minitab® (Minitab Inc. State College, Pennsylvania USA).

RESULTS

During the period 1984 through 1992, TMMC staff admitted and examined 207 (89 males and 118 females) cases of NESSD in northern elephant seals. Approximately half (44 of 87) the seals with mild NESSD were admitted during the months of December through February (Fig. 3). The peak admission months for moderate and severe NESSD cases, with 94 of the 120, were March through May. Only 17 of the total 207 seals with NESSD

were admitted during the months of July through November.

Thirty-five northern elephant seals over the age of 1 yr were admitted to TMMC in 1992. Of those, 30 (86%) had gross lesions characteristic of NESSD. Twenty-nine of the affected seals were yearlings, and one was a 2 yr old male. Seven of the diseased seals carried tags indicating birth at Año Nuevo State Reserve, California, and two from Southeast Farallon Island (37°42'N 123°O'W), California. Affected seals were recovered from nine counties in California, encompassing the entire range served by TMMC, from the California-Oregon border (40°0'N 124°1'W) through San Luis Obispo County (34°55'N 120°40'W).

Among 30 affected individuals in 1992, the mortality was one of 14 for mild cases, two of six of moderate cases, and all seven severe cases. The remaining seals were released following symptomatic therapy, supportive care and apparent recovery determined by resolution of gross lesions, normal hematologic profiles, vigorous appetite and improved body condition.

In the 1992 study, 11 species of bacteria and one fungus were isolated from the aerobic skin cultures from NESSD seals and five from normal seals (Table 1). No growth of microorganisms was obtained from the anaerobic culture skin swabs from three normal and three diseased seals.

Using a *t*-test, northern elephant seal skin disease seals had significant ($P < 0.01$) hematological changes compared to normal seals. These consisted of elevations in red blood cell count, hemoglobin, packed cell volume, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), gamma glutamyl transpeptidase (GGT), blood urea nitrogen (BUN) and uric acid, and depression of mean corpuscular hemoglobin, T4, T3, retinol, serum iron, albumin, calcium and cholesterol (Tables 2, 3).

Skin biopsies from nine of 10 affected seals had similar histopathologic lesions characterized by marked hyperkeratosis of the surface and follicular epithelium, marked acanthosis, and marked sebaceous gland squamous metaplasia and atrophy (Fig. 4). Infundibular hyperkeratosis (follicular keratosis) was observed in seven of the 10 affected individuals, while dilation of the follicle by excessive amounts of laminated keratin occurred in four cases. Mineralized cellular debris from degenerative and necrotic sebaceous cells, was observed within dilated sebaceous glands. The changes were suggestive of early transformation of the pilosebaceous units into keratin cysts. Eyelids from five of 10 of NESSD seals had moderate to marked acanthosis, follicular keratosis, and follicular dilation. Squamous metaplasia in the Meibomian glands was not observed.

Secondary skin lesions observed in affected individuals were suppurative inflammation (five cases), epidermal ulceration (four cases), intracorneal pustules (four cases), nonsuppurative inflammation (three cases), dermal fibrosis (two cases),

TABLE 1. Microbial aerobic isolates from the skin of 14 apparently normal, free-ranging yearling northern elephant seals and 15 seals with northern elephant seal skin disease in California from February to June 1992.

Isolate	Diseased	Normal
Sample size	15	14
Bacteria		
Moraxella phenylpyruvica	6	9
Proteus sp.	5	2
β-hemolytic *Streptococcus* sp.	5	1
Eschericia coli	4	0
Corynebacterium sp.	3	4
Staphylococcus sp.	2	1
Actinomyces sp.	4	0
Pseudomonas sp.	1	0
Enterobacter sp.	2	0
Klebsiella sp.	2	0
Citrobacter sp.	1	0
Fungi		
Porphyromonas sp.	1	0
No growth	0	1
Total isolates	32	18

TABLE 2. Hematological findings in 14 clinically normal, free-ranging yearling northern elephant seals and 30 seals with northern elephant seal skin disease in California from February to June 1992.

Constituent	Diseased seals		Normal seals		*P* value
	Range	Mean ± SE	Range	Mean ± SE	
White blood cells ($\times 10^3$ ml $^{-1}$)	3.0–24.5	12.7 ± 1.02	4.6–13.1	9.7 ± 0.67	NS[a]
Red blood cells ($\times 10^6$ ml $^{-1}$)	2.41–3.80	2.90 ± 0.07	1.98–2.78	2.40 ± 0.07	0.0001
Hemoglobin (gram%)	20.1–39.4	26.2 ± 0.74	20.1–25.4	22.3 ± 0.48	0.001
Packed cell volume (%)	51.5–88.3	63.8 ± 1.48	47.1–66.7	56.3 ± 1.85	0.004
Mean corpuscular hemoglobin (pg)	197.4–238.6	220.2 ± 2.18	212.2–248.8	234.4 ± 3.09	0.0005
Mean corpuscular volume (fl)	74.0–116.5	90.5 ± 2.06	84.8–106.1	93.0 ± 1.59	NS
Mean corpuscular hemoglobin concentration (g/dl)	31.1–54.7	40.9 ± 1.01	36.9–45.4	39.7 ± 0.72	NS

[a] NS: not significant at $P < 0.01$.

trichogranuloma (one case), and epidermal erosion (one case). Many of these lesions contained numerous large colonies of coccoid bacteria. There was no evidence of inclusion bodies that may be indicative of viral infections.

Pathology slides of skin specimens collected at post-mortem examination from an additional 16 cases examined from 1986 to 1992 were re-examined histopathologically. Lesions included: ulcerative dermatitis (two cases); hyperkeratosis (13); acan-

TABLE 3. Serum biochemical constituents in normal, free-ranging yearling northern elephant seals and seals with northern elephant seal skin disease in California from February to June 1992, and significance of difference between the two.

Constituent	Diseased seals			Normal seals (n = 14)		*P* value
	Sample size	Range	Mean ± SE	Range	Mean ± SE	
Retinol (μg/dL)	17	18–35	27.3 ± 1.3	25–52	34.6 ± 2.0	0.004
Total T3 (μg/dL)	13	22–60	42.5 ± 2.9	51–125	86.9 ± 5.4	0.0001
Total T4 (μg/dL)	20	0.5–2.3	1.1 ± 0.1	2.4–6.7	3.2 ± 0.3	0.0001
Sodium (mEq/L)	30	124–174	146 ± 1.5	140–153	144 ± 0.8	NS[a]
Potassium (mEq/L)	27	3.2–6.5	4.8 ± 0.1	3.7–4.7	4.3 ± 0.7	NS
Glucose (mg/dL)	30	27–247	163 ± 7.9	91–168	134 ± 5.1	0.02
Blood urea nitrogen (mg/dL)	30	18–105	39 ± 3.9	9–38	24.2 ± 2.2	0.02
Creatinine (mg/dL)	30	0.6–4.1	1.0 ± 0.1	0.8–1.8	1.2 ± 0.08	NS
Uric acid (mg/dL)	30	0.8–2.5	1.4 ± 0.07	0.7–1.1	0.9 ± 0.03	0.0001
Calcium, adjusted (mg/dL)	30	7.5–10.6	9.6 ± 0.1	10.1–11.8	11.0 ± 0.2	0.0001
Phosphorus (mg/dL)	29	5.6–16	8.2 ± 0.4	6.1–8.5	7.2 ± 0.2	NS
Total protein (g/dL)	30	2.3–9.1	8.1 ± 0.2	6.7–8.2	7.6 ± 0.1	NS
Albumin (g/dL)	30	1.8–4.3	3.1 ± 0.1	3.1–4.3	3.7 ± 0.1	0.0001
Globulin (g/dL)	30	4–10.2	5.4 ± 0.2	3.1–4.6	3.9 ± 0.1	NS
Total bilirubin (mg/dL)	30	0.2–11.2	1.4 ± 0.5	0.3–0.9	0.6 ± 0.1	NS
Alkaline phosphatase (IU)	30	60–921	334 ± 44	67–862	223 ± 55	NS
Lactate dehydrogenase (IU)	29	325–989	535 ± 25	179–517	296 ± 25	0.0001
Aspartate aminotransferase (IU)	30	35–198	86 ± 6	25–87	42 ± 5	0.02
Alanine aminotransferase (IU)	30	26–198	60 ± 7	9–68	33 ± 5	0.02
Gamma glutamyl transpeptidase (IU)	30	15–147	49 ± 7	11–46	27 ± 3	0.02
Cholesterol (mg/dL)	29	166–341	246 ± 9	170–446	332 ± 22	0.0002
Triglycerides (mg/dL)	30	32–1,277	177 ± 47	40–251	85 ± 13	NS
Iron (μg/dL)	28	32–200	106 ± 9	96–257	174 ± 12	0.0001

[a] NS: not significant at $P < 0.025$.

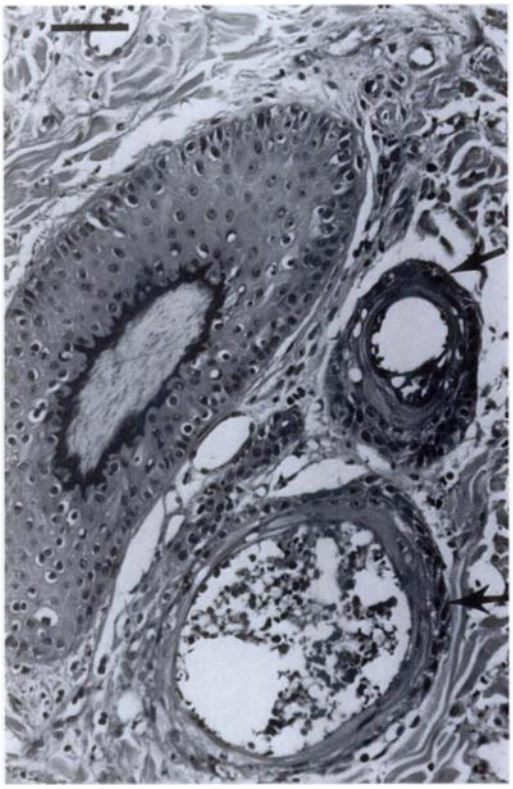

FIGURE 4. Photomicrograph of affected northern elephant seal skin with squamous metaplasia (arrows) of sebaceous glands adjacent to a hair follicle. H & E. Bar = 50 μm.

thosis (10); sebaceous gland squamous metaplasia or atrophy (14); suppurative panniculitis (four); epidermal necrosis/thrombosis of dermal vessels (five); intralesional fungal elements (five); corneal pustules (one); and sebaceous adenitis (one).

Diseased seals were approximately 15% smaller in cranial circumferences, standard length, tarsal circumferences, and mass, when compared with normal seals by sex (Table 4).

The ΣDDT in ng/g lipid weight basis consisted of approximately 98% p,p'-DDE. The diseased seals had significantly elevated mean serum ΣPCB and ΣDDT, and blubber ΣDDT. Blubber ΣPCB (Table 5) was elevated, but not significantly so. Using rank correlations of body mass with contaminant concentration, there was a strong ($P < 0.025$) negative correlation between body mass and serum ΣPCB ($r = -0.75$) and ΣDDT ($r = -0.80$). Blubber concentrations of contaminants had a weak negative correlation with mass (ΣDDT, $r = -0.62$ and ΣPCB, $r = -0.47$). Serum percent lipids were found to be positively correlated ($r = 0.59$) to body mass.

DISCUSSION

We have described a disease observed in juvenile northern elephant seals that is characterized by an ulcerative dermatitis with alopecia, hyperkeratosis and squamous metaplasia of sebaceous glands. The etiology of this potentially fatal disease was not determined despite an extensive diagnostic investigation. However, an association between NESSD and exposure to PCBs could not be ruled out.

Affected individuals suffered from clinical dehydration, emaciation, depression and bacterial infections. Hemograms were typical of stress leukograms or, occasionally, septic shock (Bossart and Dierauf, 1990).

No single microbial agent was consis-

TABLE 4. Morphometric measurements of 14 normal, free-ranging yearling northern elephant seals and 10 seals with northern elephant seal skin disease in California from February to June 1992.

	Diseased males	Diseased females	Normal males	Normal females
Sample size	4	6	5	9
Body mass	96 ± 40[a]	89 ± 21	166 ± 32	138 ± 35
Standard length	157 ± 6[b]	158 ± 6	186 ± 8	175 ± 8
Cranial circumference	66 ± 6[b]	61 ± 4	79 ± 4	73 ± 4
Tarsal circumference	43 ± 3[b]	47 ± 5	53 ± 6	51 ± 4

[a] Mean ± SD in kg.
[b] Mean ± SD in cm.

TABLE 5. Serum and blubber percent lipid, sum polychlorinated biphenyls (ΣPCB) and sum dichloro-diphenyl-trichloroethane (ΣDDT, 98% p,p'-dichloro-diphenyl-dichloroethylene) in ng/g lipid weight in normal, free-ranging yearling northern elephant seals and seals with northern elephant seal skin disease in California from February to June 1992.

	Diseased seals			Normal seals		
Constituent	Sample size	Mean ± SE	Range	Sample size	Mean ± SE	Range
Serum ΣDDT	8	9,448 ± 3,049[a]	3,370–29,700	14	2,476 ± 468	893–6,080
Serum ΣPCB	8	5,826 ± 1,914[a]	2,110–18,800	14	1,475 ± 192	795–2,950
Blubber ΣDDT	10	7,006 ± 1,257[b]	2,730–11,800	14	3,731 ± 361	1,880–6,010
Blubber ΣPCB	10	2,117 ± 406	860–4,270	14	1,087 ± 59.0	720–1,450
Serum % Lipid	8	0.86 ± 0.06	0.52–1.03	14	0.99 ± 0.04	0.74–1.26
Blubber % Lipid	10	65.68 ± 3.7	37.2–88.0	14	69.7 ± 3.5	52.5–88.7

[a] Highly significant elevation at $P < 0.01$.
[b] Marginally significant elevation at $P < 0.05$.

tently isolated from affected animals. Several bacteria appear to be normal constituents of elephant seal skin flora, including *Moraxella phenylpyruvica*, *Proteus* spp., *Corynebacterium* spp., *Staphylococcus* spp. and *Streptococcus* spp. The proliferative epithelial changes observed in NESSD may have altered the normal physiochemical and mechanical protective properties of the skin, and predisposed them to secondary bacterial and fungal infections. In addition, many of the affected individuals were debilitated and may have been immunologically compromised. Frequently, the primary cause of death was septicemia and the pathogens likely gained entry through the ulcerated dermis although the portal of entry may have been the gastrointestinal or respiratory tract in a few cases.

Northern elephant seals molt in northern California between March and May (LeBoeuf and Laws, 1994); yet all moderate and severe cases of NESSD which were observed between March and May had a virtual absence of a granular cell layer in the epidermis which is consistent with a non-molting stage of the epidermal cycle (Ling, 1972). The peak of mild cases coincided with the December to February breeding season (LeBoeuf and Laws, 1994).

Widespread epithelial hyperplasia and infundibular hyperkeratosis with mild follicular keratosis are non-specific lesions, but when observed with squamous metaplasia of sebaceous glands, have been associated with exposure to polyhalogenated aromatic hydrocarbons (PHAHs) which include PCBs and polybrominated biphenyls (PBBs) in humans, cattle, rodents, rabbits and non-human primates (Zinkl, 1977; Klein-Szanto et al., 1991, Jubb et al., 1993). The transformation of sebaceous glands into squamous cysts is considered pathognomonic for PHAH exposure in humans, and is therefore of the greatest diagnostic value (Crow, 1991). Chlorinated naphthalene exposure in cattle also causes marked hyperkeratosis of surface epithelia and follicular keratosis accompanied by additional changes of squamous metaplasia in the glands of the alimentary tract, seminal vesicles, and kidney (Jones and Hunt, 1983). Although squamous metaplasia of eyelid Meibomian glands is a feature of PCB and PBB toxicoses in some other species (Urabe and Koda, 1976), it was not observed in any of the elephant seals in this study. Bergman and Olsson (1985) observed an ulcerative dermatitis in grey seals from the Baltic Sea and suggested an association with PCBs and related chemicals.

Hormones secreted by the thyroid gland play an integral role in the health of the skin and regulation of the molting process of seals (Riviere et al., 1977; Worthy et al.,

1987). Although thyroid hormones were significantly lower in the diseased individuals, the skin lesions were not typical of those seen in cases of hypothyroid dermatopathies described in other species (Scott, 1982). Microscopic lesions were not detected in four NESSD seal thyroid glands examined histologically between 1986 and 1992. Depressions in T3 and T4 levels could have resulted from other factors such as chronic malnutrition, severe illness, or stress (Ferguson, 1988; St. Aubin et al., 1996). Polychlorinated biphenyl toxicosis can also effect the thyroid directly and indirectly. In seals and rats, exposure to PCBs has been associated with colloid depletion and thyroid fibrosis (Byrne et al., 1987; Brouwer et al., 1989; Schumacher et al., 1993). Hydroxy metabolites of certain PCB congeners interfere with plasma transport protein complexes and binding sites for retinol and thyroid hormones (Brouwer et al., 1988; Brouwer, 1991). Polychlorinated biphenyls may also affect hypothalamic secretion of thyroid stimulating hormone and lead to decreased circulating T3 and T4 (Fuller and Hobson, 1986).

Serum retinol was significantly depressed in the diseased seals and the occurrence of hyperkeratotic skin lesions and increased susceptibility to infectious agents are classic responses to retinol deficiencies in mammals (Pitt, 1985). However, strictly nutritional vitamin A deficiency is not known to cause squamous metaplasia of sebaceous glands (Gross et al., 1992; Jubb et al., 1993). Wallach and Boever (1983) mentioned a vitamin A responsive pustular dermatitis in a walrus (*Odobenus rosmarus*) presumably fed a vitamin A deficient diet. Since whole fish are high in retinol (Dierenfeld et al., 1991), it seems unlikely that a retinol deficiency would occur in a fish-eating mammal unless a metabolic disturbance of retinol uptake or transport occurred. Decreased plasma retinol and T4 have been documented in an uncontrolled study of harbor seals fed fish naturally contaminated with PCBs and other substances (Brouwer et al., 1989). Since PHAH exposure causes severe disturbances in vitamin A homeostasis through altered metabolic mechanisms, this may account for the vitamin A deficiency-like lesions associated with PHAH intoxication (Zile, 1992). Exposure to PCBs could thus potentially account for changes in serum retinol and thyroid hormone levels as well as skin lesions observed in NESSD seals.

The negative correlation between ΣPCB and ΣDDT in serum, and body mass probably reflects mobilization of contaminants from accumulated blubber stores. The increase in observed serum concentrations was likely caused by the partitioning of fat soluble residues from the blubber as the blubber mass and percent lipid is decreased in association with a period of fat mobilization due to a state of negative energy balance (Fuller and Hobson, 1986). An inverse relationship between blubber thickness and organochlorine concentration in blubber has been observed in some marine mammals (Drescher et al., 1977; Aguilar, 1983; Addison, 1989). Compared to blubber levels reported by European researchers for exposed juvenile phocid seals over the last two decades (Bowes and Jonkel, 1975; Drescher et al., 1977; Helle et al., 1983; Perttilä et al., 1986; Laws et al., 1989), the summed levels of chlorinated contaminants found in the diseased elephant seal cohort were relatively low but congener specific toxic equivalency factors were not evaluated.

A genetic component to the pathogenesis of NESSD is a possibility, but the keratinous cysts in NESSD are not analogous to the follicular comedones described in congenital keratinization defects in other species (Gross et al., 1992). The northern elephant seal population has little genetic diversity due to the population "bottleneck" created by over-harvesting (Lehman et al., 1993). Northern elephant seal skin disease is a common condition among stranded juvenile elephant seals along the California coast but the incidence in the

wild population is unknown. The severe lesions seen in this disease often produce a quick response by the general public which increases the likelihood of rescue, but also artificially inflates the prevalence.

A number of non-specific hematologic, serum biochemical and metabolic changes are associated with NESSD. These changes simply may reflect the moribund or stressed condition of the seals. Further work is needed to elucidate the respective roles of genetic, physiologic, infectious and environmental contaminants in the pathogenesis of this disease. Thyroid function tests, liver retinol determinations, and congener specific OC analyses with calculation of toxic equivalency factors are some suggested directions for future research.

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