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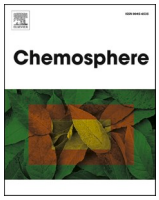

Was the massive increase in use of teratogenic agrichemicals in western states (USA) associated with declines in wild ruminant populations between 1994 and 2013?

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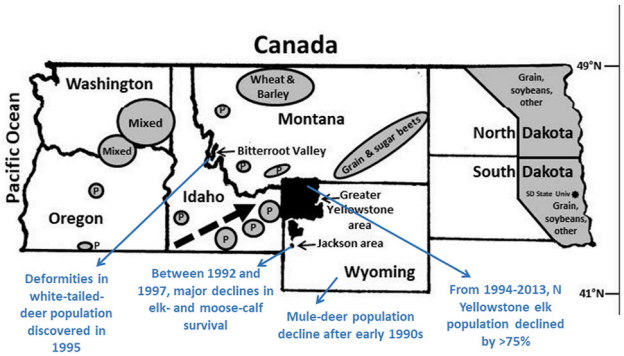
HIGHLIGHTS

- Teratogenic agrichemical use (imidacloprid, chlorothalonil, and glyphosate-based herbicides) increased regionally in 1994–96.
- Vitality of *Cervus canadensis* calves declined between 1990–92 and 1997–99 in central Wyoming.
- Calf/cow ratios in *Alces alces* declined in central Wyoming beginning in the mid-1990s.
- Reproductive abnormalities and underdeveloped facial bones were discovered in *Odocoileus virginianus* fawns in spring 1995.
- Similar abnormalities and reduced vitality were found in *Odocoileus virginianus* experimentally exposed to imidacloprid.

GRAPHICAL ABSTRACT



Major increases in teratogenic agrichemicals
1993-94: 10-fold increase in chlorothalonil due to potato-blight outbreak (P=potato fields).
1994: major neonicotinoid insecticide, imidacloprid, newly registered.
1996: 4-fold increase in herbicides with release of Roundup® Ready crops.

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ABSTRACT

Population declines were documented in multiple ruminant species in Montana and surrounding states starting in 1995. While weather, food sources, and predation certainly contributed, the declines were often attributed, at least partly, to unexplained factors. Use of teratogenic agrichemicals, notably neonicotinoid insecticides, fungicides, and glyphosate-based herbicides, massively increased regionally in 1994–96. The question explored in this review is whether this vastly increased use of these teratogenic pesticides might have contributed to observed population declines. We provide references and data documenting that specific developmental malformations on vertebrates can be associated with exposure to one or more of these agrichemicals. These pesticides are known to disrupt thyroid and other hormonal functions, mitochondrial functions, and biomineralization, all of which are particularly harmful to developing fetuses. Exposures can manifest as impaired embryonic development of craniofacial features, internal and reproductive organs, and

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musculoskeletal/integumental systems, often resulting in reproductive failure or weakened neonates. This paper reviews: a) studies of ruminant populations in the region, especially elk and white-tailed deer, prior to and after 1994; b) published and new data on underdeveloped facial bones in regional ruminants; c) published and new data on reproductive abnormalities in live and necropsied animals before and after 1994; and d) studies documenting the effects of exposures to three of the most applied teratogenic chemicals. While answers to the question posed above are complex and insufficient evidence is available for definitive answers, this review provides ideas for further consideration.

1. Introduction

This review was motivated by recognition, based on individual observations, subsequent investigations, and searching the scientific literature, that a series of seemingly unrelated events that occurred in the 1990s may have had profound effects on wild ruminants in the western United States. The initial event was a discovery, in spring 1995 in the Bitterroot Valley of western Montana, USA (Fig. 1). Multiple individual ruminants with facial malformations were observed and reproductive malformations were discovered in male white-tailed deer (*Odocoileus virginianus*) fawns. This discovery and subsequent documentation and analyses of reproductive and facial abnormalities through the 1990s and 2000s, were published by Hoy et al. (2002, 2011, 2015). An unrelated event was the release of 14 Gy wolves (*Canis lupus*) into Yellowstone National Park in March 1995. Between 1994 and 1997–98, the winter counts of the population of northern Yellowstone elk (*Cervus canadensis,* internationally known as Wapiti) declined by one third (Eberhardt et al., 2010; Mosley and Mundinger, 2018); the 2013 winter counts indicated declines of more than 75% over two decades (Fig. 2). The release of wolves was controversial from the onset, and the decline in the elk population was widely blamed on the wolves (White and Garrott, 2005), though most scientific investigations concluded that unknown or unexplained factors were likely involved.

Another series of events, seemingly unrelated to deer, elk, wolves, or Yellowstone National Park, occurred in the early-to mid-1990s that we suggest provides important clues to understanding the decline in ruminant populations in the region after 1994. In 1992–1993, summers were cooler and wetter than normal nearly worldwide following the massive eruption of Mt. Pinatubo in June 1991 (Self et al., 1996). The cool, wet conditions contributed to outbreaks of the pathogenic fungus *Phytophthora infestans* (late blight) in major potato-growing areas, spreading to Idaho and eastern Washington by 1993–94 (Fry and Goodwin, 1997). The consequent increase in the use of fungicides, notably chlorothalonil, in Idaho, Washington, Oregon and, by 1996, Montana, was substantial (Thelin and Stone, 2013; see also https://water.usgs.gov/nawqa/pnsp/usage/maps/about.php). Also in 1994, a neonicotinoid insecticide, imidacloprid, was registered for use and has since become the most heavily applied insecticide throughout the United States (U.S. National Pesticide Information Center, http://npic.orst.edu/factsheets/imidagen.html). Then in spring 1996, the introduction of Roundup® Ready crops resulted in major increases, by thousands of metric tons, in the already widespread use of glyphosate-based herbicides (GBHs) (USGS National Water Quality Assessment).

In this review, we examine evidence that exposure to these three kinds of teratogenic agrichemicals: chlorothalonil, imidacloprid, and GBHs (e.g., Cerrizuela et al., 2020), in vastly increased concentrations beginning in 1994, should be considered as possible factors that contributed to the unique congenital malformations and increased mortality in young of multiple ruminant species. We propose that failure to thrive and the subsequent prenatal and neonatal mortality may have contributed to declines in wild ruminant populations. As evidence, we discuss experimental studies that report how exposure to these agrichemicals have been directly linked to a variety of congenital malformations, including facial and reproductive malformations in white-tailed deer (Berheim et al., 2019).

The elk populations of the Greater Yellowstone ecosystem have been frequently studied, with data available from both prior to 1994 and after. Thus, Section 2 summarizes studies of elk populations in the region. In Section 3, we review observations and reports, which emerged after 1994, of birth defects and declines in other ruminant populations in western states. In Section 4, we discuss the specific kinds of agrichemicals for which use increased dramatically in the region in the mid-1990s. These pesticides are known to disrupt thyroid and other hormonal functions, metabolic functions, and biomineralization, all of which can be particularly harmful to developing fetuses [i.e., are teratogenic in affected animals (Cerrizuela et al., 2020)]. In Section 5, we return to more recent observations of elk populations, and in Section 6, ask why the effects of new and much higher pesticide exposures, especially the serious external congenital malformations, have been so widely overlooked as possible contributors to documented declines of

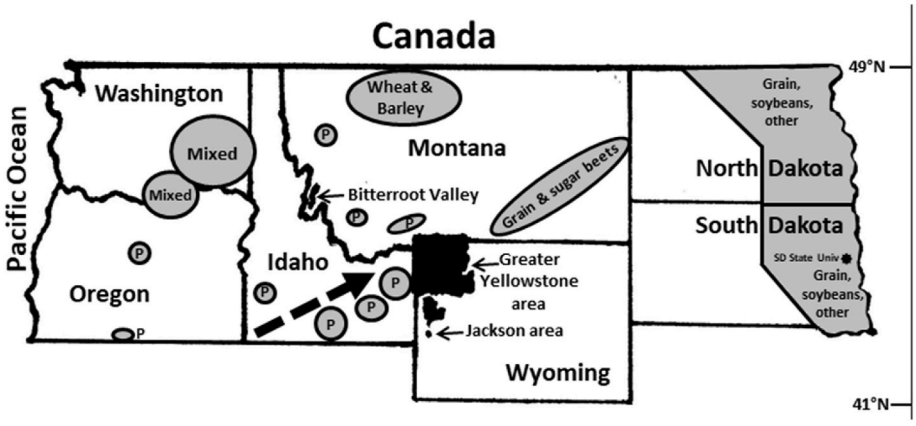

Fig. 1. Areas and locations in the west and central northern United States mentioned in the text. General regions of intensive agriculture are noted (P indicates major potato-growing areas), as is the prevailing southwest wind direction influencing the Greater Yellowstone area (heavy dashed arrow). Data sources: https://pacific-map.com/agriculture-and-industry-map-of-oregon.html; https://pacificmap.com/agriculture-and-industry-map-of-idaho.html; https://agr.mt.gov/Ag-in-the-Classroom, www.agr.wa.gov/PestFert/natresources/AgLandUse.aspx; https://www.farmflavor.com/north-dakota/north-dakota-crops-livestock/north-dakota-agriculture-map/; https://www.nass.usda.gov/Statistics_by_State/South_Dakota/Publications/County_Estimates/index.php.

ruminants. While the topics posed above are complex and insufficient evidence is available for definitive answers, our goals are to provide ideas for further consideration and study.

2. Elk and other wildlife in the Greater Yellowstone region

2.1. Historical background

Yellowstone National Park was established in 1872, the first in the United States. The park is located mostly in northwest Wyoming, extending into southwestern Montana and east-central Idaho (Fig. 1). Originally preserved for its unique hydrothermal activity and breath-taking scenery, the park also attracts visitors from around the world to see the amazing array of wildlife. These include grizzly bears (*Ursus arctos horribilis*), black bears (*Ursus americanus*), wolves (*Canis lupus*), American bison (*Bison bison*), elk (*Cervus canadensis*), pronghorn antelope (*Antilocapra americana*), bighorn sheep (*Ovis canadensis*), mountain goat (*Oreamos americanus*), moose (*Alces alces*), mule deer (*Odocoileus hemionus*), and white-tailed deer (*Odocoileus virginianus*), as well as an abundance of smaller mammals and birds. Many of these species are rare outside of American and Canadian national, state or provincial parks.

Populations of several of the charismatic larger species have fluctuated inexplicably in recent decades. For example, according to the 1994 winter count, the northern Yellowstone elk population was ~18,000. By 1997–98, the counts had dropped by about one third, to ~12,000. The decline continued, with the elk population at ~8000 in 2004 (Eberhardt et al., 2010; Mosley and Mundinger, 2018). By 2013, fewer than 4000 were recorded (Fig. 2).

What could have caused such a decline in this elk herd? What also should be asked is what may have happened in 1994 to cause several distinctive, externally observable developmental malformations to emerge among young of multiple vertebrate species in spring of 1995 and then again each spring through 2013? While answers to these questions are complex, our discussion of studies from immediately before and after 1994, as well as subsequent studies and extremely pertinent new data, provide questions for further consideration.

The gray wolf (*Canis lupus*) was extirpated from the Yellowstone ecosystem in the 1920s when the last native wolves were killed (Fischer, 1995). In January 1995, 14 Gy wolves from Canada were brought to the park and released the last week of March, with another 17 released in 1996 (Smith et al., 2019). The wolves formed packs, mated, had pups, and their population subsequently increased faster than biologists had predicted (Fischer, 1995; Boyce, 2018).

Elk in the greater Yellowstone ecosystem have been extensively studied for at least a century (Fig. 2) (Middleton et al., 2013), and wolves have had continuous surveillance since their release in 1995 (Boyce, 2018). Even though the wolf population increased quite rapidly, there were never enough wolves to cause the rate and magnitude of declines in elk and other wild ruminants in Yellowstone National Park or the region (Boyce, 2018). However, immediately after their release in Yellowstone, the wolves undoubtedly took advantage of the bountiful food supply of dead and weakened ruminants they found in their new habitat. This would have helped the wolves thrive, providing an explanation for why their population initially grew so rapidly (Smith et al., 2019).

2.2. Elk population studies

A crucial, multi-year study of elk calves was carried out near Jackson, in west-central Wyoming (Smith et al., 2006), south of Yellowstone National Park (Fig. 1). In the first three-year study period, 145 neonatal elk from three cohorts (1990, 1991, 1992) were captured, radio-instrumented, and monitored for survival. The elk calves were reported as healthy and energetic, and joined the nurse herd at an average of 12 days of age. After joining the herd, the calves were much less susceptible to being caught by grizzly bears, black bears, coyotes (*Canis latrans*), or mountain lions (*Puma concolor*), the predators at that location and time. No calves older than 12 days of age were recorded as killed by predation. By 30 days after birth, the survival curve for the calves flattened at ~85%, with 22 recorded deaths (Smith et al., 2006).

For the second period of their study, the team captured and radio-instrumented 153 neonates from three cohorts (1997, 1998, 1999). Those calves, especially females, were smaller, gained weight more slowly, and their blood chemistries indicated reduced nursing. The calves were vulnerable to mortality, especially predation, as much as four times longer than the calves monitored in 1990–92. For the 1997–99 cohorts, the survival curve flattened at ~72% by 60 days after birth with 42 total deaths. The study concluded that postpartum conditions for neonates had declined by the late 1990s. As a result, newborns grew more slowly, extending the time during which the calves were vulnerable to mortality, particularly predation (Smith et al., 2006).

Thus, the neonatal elk calves captured and radio-instrumented in

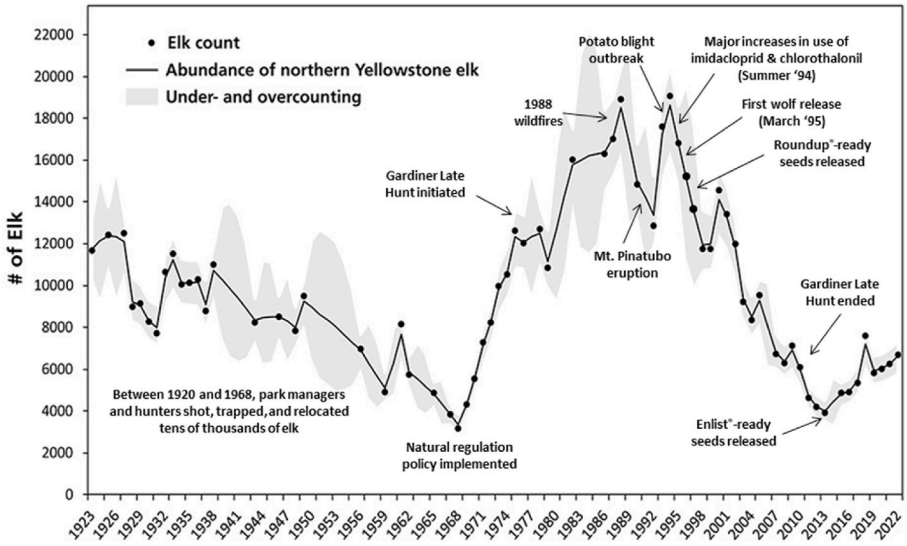

Fig. 2. Counts (circles) and fitted trend line for abundance of the northern Yellowstone elk herd, 1923–2015. Shaded area indicates uncertainty in the trend. Data are from the Northern Yellowstone Cooperative Wildlife Working Group. Figure adapted from MacNulty et al. (2016) and information therein, with events described in this review also noted.

1997–99 exhibited reduced nursing, slower growth, and decreased activity levels, resulting in nearly double the loss to predation compared to those observed in the 1990–92 cohorts. Three of the non-predation causes of death in the 1997–99 calves were attributed to difficult births or heart defects. The authors suggested that the increased neonatal mortality in the 1997–99 calves could have resulted from cooler spring weather and slower greening of pastures. However, the only neonatal deaths from emaciation and starvation were recorded in 1990 and 1991 (Smith et al., 2006).

The study by Smith et al. (2006) also noted that the decline in neonatal-calf survival reduced the annual growth rate of the Jackson elk herd by an annual increment of approximately 500 animals in a pre-parturition herd of 11,000 elk. Moreover, mid-summer surveys of calf/cow (adult-female) ratios in 1997–99 indicated a 39–45% greater decline in neonatal survival even than measured among the radio-instrumented calves. The research team suggested that increased predation resulted from predator selection of inferior calves and increased mortality of individuals with reduced first-week growth rates. Those differences in the health and survival of newborn elk calves of the same herd in the two study periods provide critically important information regarding changes in neonatal vitality and survival.

No adequate explanations were given for the major difference in elk-calf health and mortality between the two three-year intervals of the study. What could have happened in the mid-1990s to cause such a remarkable difference in the results? We suggest that answers to that question are essential to understanding the declines in elk and other ruminant populations in the years after 1994. When reading the contrasting results of the two assessment periods (1990–92 and 1997–99) (Smith et al., 2006), we noted that the second study period occurred following the massive increases in regional use of teratogenic agrichemicals.

Other studies of elk populations in the Greater Yellowstone Ecosystem reported high mortality and low calf/cow ratios in most years after 1994 (White and Garrott, 2005; Barber-Meyer et al., 2008; Eberhardt et al., 2010; Middleton et al., 2013). A study from 1989 to 2009 compared survival rates of calves in the migratory herd with the resident herd (Middleton et al., 2013). In the migratory herd, which summers further west in the park, winter calf recruitment declined from 30 to 40 calves/100 cows in 1990–94 to 10–15 calves/100 cows in 2009. In the resident elk herd, winter calf recruitment declined by roughly half between 1994 and 2002 (~40 calves to ~20 calves/100 cows), increasing back to original ratios by 2009. Other studies also noted declines in juvenile/cow ratios (Smith et al., 2006; Christianson and Creel, 2014; MacNulty et al., 2016)). In 2003–04, the summer survival rate in Yellowstone elk calves was less than half that found in a similar three year study in 1987–1990 (Vucetich et al., 2005), despite a large forest fire and a severe winter in 1988 (Fig. 2). Boyce (2018), based on their 2003–2005 study of elk calf survival and mortality, suggested that adverse effects on the calves' immune systems (e.g., low levels of gamma gobulin) were possible factors that affected survival.

A subsequent study examined 33 years of data from twelve populations of elk in southwestern Montana and northwestern Wyoming before and after the wolves were released (Christianson and Creel, 2014). While substantial decreases in elk numbers occurred immediately after the wolves were released and expanded their territory, the authors considered the additive effects of wolf predation on elk survival to have been relatively weak. Moreover, there were no wolves in the Jackson area where the Smith et al. (2006) study was conducted.

2.3. The wolf population in the yellowstone ecosystem

The wolf population increased rapidly following the release of 14 adults in 1995 and 17 in 1996. No wolves with birth defects were reported in Yellowstone. By 1998, there were 112 wolves and by 2003 there were 174 wolves, with 59 surviving pups (Smith et al., 2019). The population remained at that level through 2007 when there were 171 wolves, with 64 surviving pups. Mange was detected in the population in 2007, with only 22 pups surviving in 2008; in subsequent years (to 2019), the number of surviving pups per year averaged around 31 (Smith et al., 2019; Smith). The overall population stabilized at around 100 wolves in ten or eleven packs. With a maximum of 20–22 elk killed per adult wolf per year, a population of 70 adults and 30 pups would be responsible for approximately 1500 elk deaths each year (Smith). If reduced neonatal vitality and higher mortality had not been affecting elk starting in the mid-1990s, sufficient numbers of calves should have survived each year to maintain stable populations, even with increased numbers of wolves and grizzly bears (Singer et al., 1997; Griffin et al., 2011; Christianson and Creel, 2014).

In years prior to 1995, approximately 33 calves/100 cow elk were reported in several studies (Singer et al., 1997; Vucetich et al., 2005; Eberhardt et al., 2010). In spring 1995 and for almost two decades thereafter, fewer than 20 calves/100 cows became the norm (Smith). These decreases in calf survival are an example of what researchers have referred to as "unexplained declines" (e.g., Middleton et al., 2013; Christianson and Creel, 2014). One reason suggested for the failure of elk cows to conceive was that being chased by wolves caused decreased progesterone levels (Creel et al., 2007). However, disruption of progesterone levels and other endocrine functions in mammals can also be caused by pesticide exposure (Bretveld et al., 2006; Kapoor et al., 2011), which was not previously considered. In a study of neonatal elk-calf mortality in 2003–2006, wolves reportedly caused 14–17% of the elk-calf mortalities compared to 58–60% attributed to bears (Garrott et al., 2009). Wild ruminants weakened perinatally typically die during their first year, whether killed by predators or consumed after they die (Singer et al., 1997).

Numerical support for our suggestion that wolves were not major contributors to declines in elk populations is based upon how many elk are known to be killed and eaten by an adult wolf. Yellowstone wolf researcher, Doug Smith, was quoted as follows: "Over the course of a year, an average wolf will kill—mostly with other pack members—and consume 16 to 22 elk a year" (Thuermer, 2017, p. 1). Thus, the most elk 14 wolves would likely have killed in the first year after their release in late March 1995 was ~300. And, as noted above, a population of 70 adult wolves and 30 pups likely would be responsible for approximately 1500 elk deaths each year (Smith).

3. Observations of other ruminant species

Long-term trends reported by state game departments from prior to 1995 through 2013 noted that the number of juveniles/100 adult females in wild ruminant herds decreased starting in 1995–1996 (Vucetich et al., 2005). Studies of neonatal white-tailed deer indicate that fawns with adverse health issues or in poor condition are targeted by predators (Mech, 2007; Carstensen et al., 2009). Reports of birth defects and declines in other ruminant populations in western states also emerged after 1994. Affected taxa include mule deer (Hutto, 2013; Ellenberger and Byrne, 2015; Hansen, 2020), pronghorn antelope (White et al., 2007), bighorn sheep (Enk et al., 2001), mountain goat (Koeth, 2008) and white-tailed deer (Hoy et al., 2002, 2011).

Similar declines were documented in moose populations in Montana and Wyoming (Nadeau et al., 2017), associated with reduced survival of young. For example, the moose population in the Jackson, Wyoming area also declined after 1995. The moose calf/100 cow ratios declined from a 1963–1993 average of 48 calves/100 cows to a 1998–2003 average of 34:100 (Brimeyer and Thomas, 2004). That study concluded that the reason for reduced calf production was low pregnancy rates and low twinning rates. Importantly, this decline occurred in the general area of the definitive study of neonatal elk calves (Smith et al., 2006).

Mule deer often share elk habitat. The Mule Deer Working Group for the Western Association of Fish and Wildlife Agencies (Hansen, 2020) reported that mule-deer populations throughout Wyoming declined after the early 1990s. Fawn productivity, on average, decreased

statewide by about 15%, and since 2000, mule-deer populations have declined by an estimated 42%.

The decline of the bighorn-sheep herds in the Canyon National Recreation Area and Pryor Mountain wild horse range east of Yellowstone National Park on the southern Montana/northern Wyoming border provides another example (Kissell et al., 1996). Following the release of new sheep in 1973, with growth rates near maximum potential of 20% per year, the population grew to an estimated peak population of about 211 animals in 1993 and 1994, then began to rapidly decrease in 1995 and 1996. One hypothesis for the decline was that stressed bighorn sheep are apparently more susceptible to pneumonic *Pasteurellosis* than those not stressed (Kraabel and Miller, 1997).

Scientists concerned with wild ruminant populations should consider that the species with the above referenced declines began being born with an increased prevalence of uniquely underdeveloped facial bones beginning in 1995 (Hoy et al., 2011).

3.1. White-tailed deer

White-tailed deer on the Lee Metcalf National Wildlife Refuge in the Bitterroot Valley in western Montana (Fig. 1) were assessed in the winter of 1991–92 by Bart O'Gara, Ph.D., a wildlife biologist at the University of Montana. The purpose was to document birth defects and any other adverse health issues that might be associated with the overpopulation of white-tailed deer on the refuge at that time. The only health issue found among the 100 deer examined was one older doe with pneumonia. No malformations of any kind were found, including on examined fetuses. The sex ratio on 32 fetuses collected was 16 M/16F (O'Gara, 1992). This study provided crucial background data to compare with adverse health issues and unique birth defects documented on white-tailed deer born in spring of 1995 and thereafter (Hoy et al., 2002, 2011, 2015) (Table 1).

While working with wildlife in Montana (Fig. 1) for three decades prior to 1995, the lead author and a wildlife-biologist collaborator (Hoy et al., 2002, 2011), who worked for Montana Department of Fish, Wildlife and Parks from 1965 through 2000, had observed only one mammal with a birth defect. Beginning in 1995, birth defects were frequently observed, the most common were male reproductive malformations and disrupted craniofacial development (Hoy et al., 2002, 2011). Many of the white-tailed deer fawns and other newborn ruminants necropsied after being found dead, also had an inflamed or underdeveloped thymus, damaged lungs, and an enlarged right-heart ventricle (Hoy et al., 2015; Hoy, 2017).

On male white-tailed deer born in 1995 through 2018, malformed or underdeveloped genitalia were commonly observed (Hoy et al., 2002, 2011; Stone et al., 2019). These anomalies include unformed or malformed testicular hemiscrota, ectopic testicles, and underdeveloped penile sheaths (Fig. 3). A previously unreported testicular hemiscrotal condition results when one hemiscrotum occurs directly forward of the other, rather than side by side (bilateral) (Fig. 3f,g,h). The forward misplacement of the inguinal lymph node and consequent forward condition of the spermatic cord, usually on the left, results in this

Table 1
Data on facial characteristics of 1063 hunter-harvested adult, mostly male wild ruminants examined from 2006 to 2022. *2019–22 data are provided both separately and combined, the latter for ease of comparison with data from 2012 to 2015.

Species common name	Years	Number examined	Normal bite	%	Underbite	%	Overbite	%	Maloclusion total	%
C. canadensis	2006–11	46	23	50%	17	37%	6	13%	23	50%
Elk or Wapiti	2012–15	47	32	68%	14	30%	1	2%	15	32%
	2016–17	25	20	80%	4	16%	1	4%	5	20%
	2018–19	17	16	94%	1	6%	0	0%	1	6%
	2019–20	22	18	82%	4	18%	0	0%	4	18%
	2020–21	35	27	77%	3	9%	5	14%	8	23%
	2021–22	23	17	74%	4	17%	2	9%	6	26%
	2019–22*	80	62	78%	11	14%	7	9%	18	23%
	Total	215	153	71%	47	22%	15	7%	62	29%
O. hemionus	2006–11	61	20	33%	37	61%	4	7%	41	67%
Mule Deer	2012–15	45	11	24%	33	73%	1	2%	34	76%
	2016–17	39	16	41%	23	59%	0	0%	23	59%
	2018–19	27	17	63%	10	37%	0	0%	10	37%
	2019–20	41	17	41%	23	56%	1	2%	24	59%
	2020–21	36	19	53%	14	39%	3	8%	17	47%
	2021–22	33	19	58%	9	27%	5	15%	14	42%
	2019–22*	110	55	50%	46	42%	9	8%	55	50%
	Total	282	119	42%	149	53%	14	5%	163	58%
O. virginianus	2006–11	44	24	55%	11	25%	9	20%	20	45%
White-tailed	2012–15	60	25	42%	29	48%	6	10%	35	58%
Deer	2016–17	40	27	68%	11	28%	2	5%	13	33%
	2018–19	39	28	72%	7	18%	4	10%	11	28%
	2019–20	51	33	65%	13	25%	5	10%	18	35%
	2020–21	58	37	64%	7	12%	14	24%	21	36%
	2021–22	32	20	63%	5	16%	7	22%	12	38%
	2019–22*	141	90	64%	25	18%	26	18%	51	36%
	Total	324	194	60%	83	26%	47	15%	130	40%
A. americana	2006–11	48	13	27%	30	63%	5	10%	35	73%
Pronghorn	2012–15	39	11	28%	27	69%	1	3%	28	72%
Antelope	2016–17	26	6	23%	20	77%	0	0%	20	77%
	2018–19	7	3	43%	3	43%	1	14%	4	57%
	2019–20	38	10	26%	26	68%	2	5%	28	74%
	2020–21	30	9	30%	19	63%	2	7%	21	70%
	2021–22	24	6	25%	18	75%	0	0%	18	75%
	2019–22*	92	25	27%	63	68%	4	4%	67	73%
	Total	212	58	27%	143	67%	11	5%	154	73%
Bison bison	2018–20	16	8	50%	5	31%	3	19%	8	50%
American Bison	2020–22	14	9	64%	3	21%	2	14%	5	36%
	Total	30	17	57%	8	27%	5	17%	13	43%

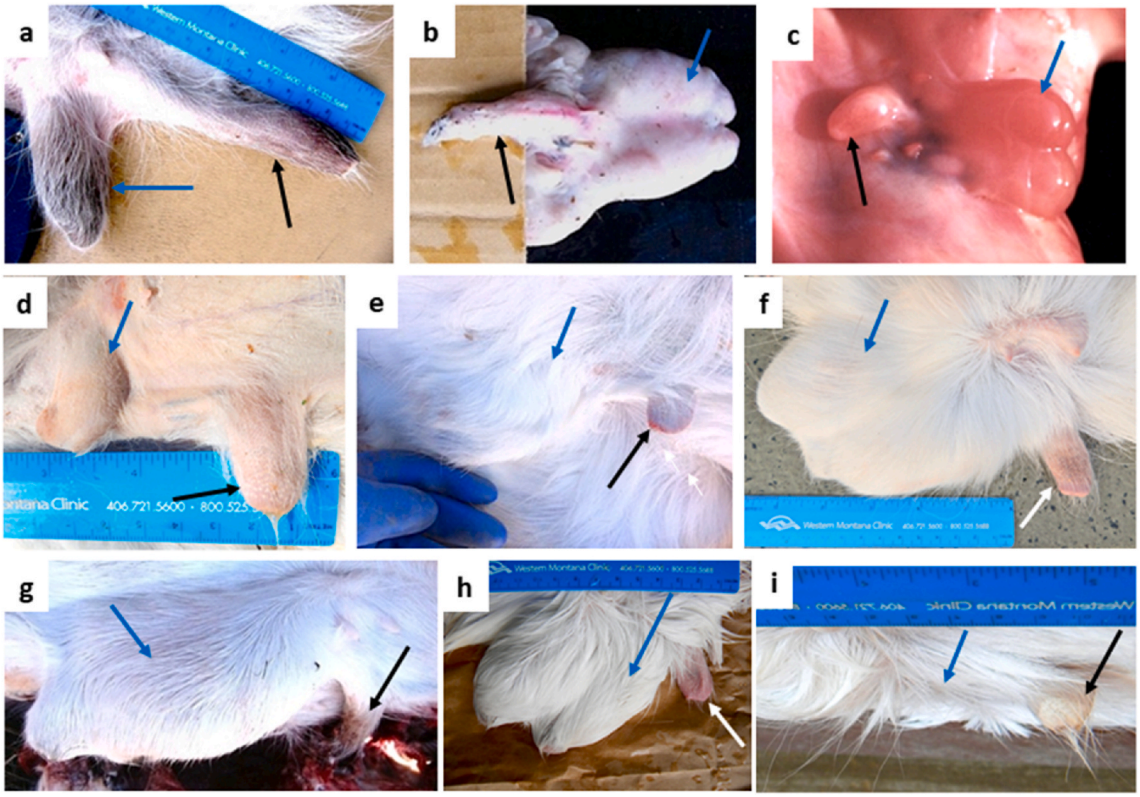

Fig. 3. Male white-tailed deer genitalia showing penile sheath conditions from normal to extremely short and a variety of scrotal shapes and conditions from normal to no hemiscrota formed.
a) Straight side view of adult genitalia with a normal-length (7 cm) bilateral scrotum (blue arrow) containing both testicles. In a side view of a normal scrotum, only one hemiscrotum is visible. The penile sheath (black arrow) is normal in length at 6.9 cm. The deer was killed in early summer, out of breeding season. A normal adult penile sheath ranges from 4.5 cm to 7.5 cm in length; on a normal full-term fetus the penile sheath typically exceeds 2.3 cm
b) Genitalia of an adult male after the external skin was carefully removed, showing the normal-length penile sheath (black arrow) and normal length (6.2 cm), bilateral testicles (blue arrow). This bilateral position of the testicles, while hanging straight down away from the heat of the body is the normal configuration for a ruminant scrotum.
c) Normal genitalia of an unhaired fetus: bilateral scrotum (blue arrow) and a normal-length penile sheath (black arrow). Mammal genitalia form during early fetal development and the genitalia configuration at birth is permanent unless altered postnatally.
d) Genitalia of a yearling with only one hemiscrotum formed, containing the right testicle (blue arrow). The left testicle is completely ectopic. The penile sheath (black arrow) is somewhat short.
e) Genitalia of an adult in which bilateral testicles were horizontal in an ectopic position (blue arrow) between the outer skin and the body wall resulting in a short bump in the skin of the groin area. The penile sheath (black arrow) is extremely short.
f) Genitalia of an adult with a scrotum formed by the left testicle dropping into a position directly forward of the right testicle during fetal development, resulting in the hemiscrota being in a misaligned position and tipped backward (blue arrow), causing testicles, especially the right testicle, to be partly ectopic and affected by the heat of the body. The penile sheath (white arrow) is within normal range.
g) Genitalia of an adult with the left testicle in a horizontal position directly forward of the horizontal right testicle (blue arrow) with both ectopic against the body, resulting in a bizarre-looking scrotum. The penile sheath (black arrow) was within normal range.
h) Genitalia of an adult with a misaligned scrotum (blue arrow) similar to the misaligned condition shown in (f), except the testicles are located away from the body wall. The penile sheath (white arrow) is short.
i) Genitalia of a yearling with both testicles horizontal between the external skin and the body wall (blue arrow) with no hemiscrota formed on the external skin. The penile sheath (black arrow) is extremely short (1.7 cm). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Fig. 4. Photos of male elk genitalia showing a) a normal bilateral scrotum and b) a tipped bilateral scrotum. c) Misaligned hemiscrota on a hunter-killed bull elk, the only dead male elk available for the authors to examine and photograph.

configuration of the scrotum to be formed on the fetal skin (Hoy et al., 2002, 2015). From 1995 and each year thereafter, in substantial proportions of males with hemiscrota either bilateral (normal position, Fig. 3a,b,c) or misaligned (Fig. 3e–i), the entire scrotum was extremely short or not formed on the external skin (Fig. 3d,e,i). When the testicles descend into a horizontal ectopic position between the skin and the body wall, usually making a short bump in the skin of the groin area, such placement results in heat-damaged sperm and infertility (Guillette and Guillette, 1996; Hamilton et al., 2016).

The observed reproductive malformations were documented by multiple measurements of the genitalia on 254 male white-tailed deer from January 1996 through March 2000 (Hoy et al., 2002). Reproductive malformations were also documented on other mammals (e.g., Fig. 4); the most common being unusual placement of the testicles resulting in misshapen hemiscrota, as well as extremely short penile sheaths on multiple rodent species and both white-tailed and mule deer (Hoy et al., 2015). Again, these congenital reproductive malformations were first documented on young born in 1995 (Hoy et al., 2002).

Another anomaly was the skewed sex ratio found on accident-killed white-tailed deer fawns born in western Montana (Hoy et al., 2002). From spring 1996 through spring 2000, 315 examined fawns included 185 males (59%) and 130 females (41%). On 330 fawns examined from 2001 to 2010, the sex ratio was 184 males (56%) to 146 females (44%). If all wild ruminant populations similarly had fewer females born, the subsequent lack of adult females to produce normal numbers of young could have contributed to the population declines reported from 1995 through 2013 (Enk et al., 2001; Ellenberger and Byrne, 2015; Nadeau et al., 2017; Hansen, 2020).

Unique craniofacial malformations also were first noted on both sexes of wild and domestic ruminants in spring of 1995. From January 1996 through December 2010, the facial anatomy of dead ruminants was quantitatively documented (Hoy et al., 2011). The bite from the extreme anterior of the dental pad to the top of the middle incisors and the width of the dental pad and width of the lower incisors were measured on 1061 white-tailed deer that were accident killed or died of natural causes, in addition to smaller samples of hunter-harvested wild ruminants (Hoy et al., 2011). The most common malformation observed was malocclusion of the incisors with the dental pad, resulting from the mismatch in the length of the mandible (lower jaw) and the maxilla (upper jaw). This malocclusion type, medically referred to as brachygnathia superior and commonly known as underbite, occurs when the lower jaw is normal in length and the premaxillary bone is underdeveloped (Schutte & van den Ingh, 1997). This malformation on ruminants results in the incisors being forward of, and usually somewhat wider than, the dental pad on the anterior of the underdeveloped premaxillary bone, and often tipped forward (Fig. 5, see also Appendix A). On mammals with both upper and lower incisors (equines, canids, etc.) that exhibit this malformation, the lower incisors are forward of the upper incisors (Hoy et al., 2011) (Fig. 5h). The malformation in mammals results from underdevelopment of the upper facial bones (e.g., Allen, 1995; Schutte & van den Ingh, 1997); on bird species the normal length lower bill is longer than the abnormally short upper bill (Handel et al., 2010; Handel and van Hemert, 2015). Prior to the study of malocclusions on wild ruminants beginning in 1996 (Hoy et al., 2011), only a few scattered reports of brachygnathia superior (underbite) were found in case studies (e.g., Barrett and Chalmers, 1975; Rollor, 1993).

The facial-bone malformation that results from the underdevelopment of the portion of the lower jaw forward of the premolars is referred to as mandibular brachygnathia, brachygnathia inferior, or overbite (Hoy et al., 2011). Overbite is more readily apparent than underbite to a casual observer (see Appendix A).

3.2. Observations of anomalies on other species

In addition to populations of elk and white-tailed deer, mule-deer populations also declined in several western states after 1994,

Fig. 5. Photographs of ungulate heads, skulls or mouths exhibiting underdeveloped upper facial bones and underbite; medically termed brachygnathia superior.
a) Elk calf (*Cervus canadensis*) with severe underbite; the premaxillary bone is underdeveloped, thus short and narrow (see also Appendix A).
b) Mule-deer fawn (*Odocoileus hemionus*) with a severe underbite, crooked teeth, and incisors much wider than underdeveloped dental pad.
c) Newborn white-tailed deer (*Odocoileus virginianus*) with severe underbite and incisors much wider than underdeveloped dental pad (see also Appendix A).
d) Domestic goat (*Capra aegagrus hircus*) with severe underbite and incisors much wider than the underdeveloped dental pad.
e) Skinned head of hunter-killed adult-male pronghorn antelope (*Antilocapra americana*) with underbite, narrow dental pad and overgrown lower incisors, all with distinctive round tops from lack of wear. Because the incisors do not contact the dental pad, the teeth do not experience normal wear. Underbite can be determined in an adult ruminant by examining the lower incisors.
f) Cleaned skull of an adult-male bighorn sheep (*Ovis canadensis*) with an underdeveloped premaxillary bone and consequent underbite, similar to the hunter-killed antelope (e).
g) Bison calf (*Bison bison*) in Yellowstone National Park showing the short, underdeveloped upper facial bones. The lower lip is forward of the upper lip, denoting an underbite. In calves with a normal premaxillary bone, the nose pad is prominently forward of the lower lip (see Appendix B).
h) Newborn foal (*Equus caballus*) with underbite to illustrate that species other than ruminants were affected.

attributed to non-survival of fawns (Unsworth et al., 1999). The same unique developmental malformations began to be observed and documented on mule deer, as well as other wild and domestic animals (Schutte & van den Ingh, 1997; Hoy et al., 2002, 2011). Heads of hunter-harvested game animals were received and examined between 2006 and 2022 by co-author GTH, a wildlife biologist and experienced taxidermist. Underdeveloped facial bones resulting in malocclusion, including either underbite or overbite, were found on 62 of 215 elk (29%), 154 of 212 pronghorn antelope (73%), 163 of 282 mule deer (58%), 130 of 324 white-tailed deer (40%), and 13 of 30 bison (44%) (Table 1). Underbite was also documented on 10 of 19 male bighorn sheep (53%) killed because of a pneumonia outbreak in western Montana in 2009.

In 1995 and thereafter, livestock owners in western Montana reported pre- and neonatal domestic animals, including sheep (*Ovis aries*), goats (*Capra hircus*), beef and dairy cattle (*Bos taurus*), and horses (*Equus caballus*), born with similar malformations and adverse health issues to those observed on wild ruminants (Hoy et al., 2002, 2011). In the late 1990s in western Canada, foals tested for thyroid-hormone disruption during fetal development were born with underbite, weakness at birth, and crooked leg bones (Allen et al., 1998). In Mexico, bovine calves, especially *Bos indicus*, were reported by a veterinarian to be born with malocclusion of the jaws, some with widely spaced lower incisors (Saiz Pineda, 2018). In domestic animal heads examined by co-author GTH between 2018 and 2022, 32 (56%) of 57 exhibited malocclusion. Thus, birth defects, especially the underdeveloped facial-bone abnormalities, should be of concern in the livestock industry.

4. Teratogenic pesticides as potential causes of birth defects and mortality

The first three years (1990–92) of the Jackson-area neonatal elk-calf study (Smith et al., 2006) occurred immediately prior to unprecedented increases in regional use of three major kinds of agrichemicals (i.e., 1994–96). Those pesticides now are recognized among the most important environmental teratogens, as they are produced and used on massive scales worldwide and are known to have profound effects on embryonic development of vertebrates (Cerrizuela et al., 2020, and references therein). In summer of 1994, the newly registered imidacloprid, a neonicotinoid insecticide, began being applied to fields in states to the west of both Yellowstone National Park and the elk-study area near Jackso n, with use rapidly increasing from none prior to 1994, to widespread heavy application by 2014 (USGS National Water Quality Assessment). Also beginning in 1994, the outbreak of late blight in potato fields in nearby Idaho, as well as in Oregon and Washington (Fry and Goodwin, 1997; Henderson et al., 2007) (Fig. 1), resulted in substantially increased use of fungicides (e.g., USGS National Agricultural Research Service, 1998). Use remained high through 2001, declining somewhat thereafter, but remaining higher than 1993 usage. Then, in 1996, the release of genetically modified Roundup® Ready seeds resulted in a four-fold increase in the use of glyphosate-based herbicides (GBHs) throughout the USA between 1996 and 2000 (e.g., National Agricultural Research Service, 1998; Benbrook, 2012). Many of the chemicals now widely used have been shown to disrupt a range of crucial biological processes from intracellular and hormonal functions to feeding efficiency and nutrient availability (Swanson et al., 2014; Gore et al., 2015; Leemans et al., 2019; Cerrizuela et al., 2020).

Hundreds of studies have explored how low-dose exposure to endocrine-disrupting chemicals can interfere with hormone-system functions in vertebrates, including humans. For example, a Web of Science search (May 25, 2023) using the topics “endocrine disruption” and “pesticide” returned >1000 references since 1993, many dealing with wildlife and humans. Effects of specific interest include disruption of sex hormones in adults of both sexes and failure of females to become pregnant (e.g., Diamanti-Kandarakis et al., 2009; Sharma and Goyal, 2014; and references therein).

Other consequences of exposure can include impaired embryonic development of the brain, eyes, heart, lungs, thymus, reproductive organs, and musculoskeletal/integumental systems (Diamanti-Kandarakis et al., 2009). Smith et al. (2006) likely were unaware of the unprecedented new regional use of chlorothalonil, imidacloprid, and GBH pesticides during the years between their monitoring intervals. Those three groups of teratogenic agrichemicals were applied in massive amounts upwind of the study area for three years before and throughout the second neonatal elk study period. Most importantly, the observed differences in the health and survival of newborn elk calves in the two study periods (Smith et al., 2006) are consistent with documentation that other vertebrate species were similarly affected (Rolland, 2000; Gibbons et al., 2015).

Moreover, the range of symptoms observed in the 1997–99 elk calves (Smith et al., 2006) and on other vertebrate young are consistent with the consequences of exposure to thyroid hormone-disrupting chemicals reported in reviews of field studies on wildlife (Rolland, 2000; Gibbons et al., 2015). Symptoms consistent with thyroid-hormone disruption (Caux et al., 1996; Rolland, 2000; Diamanti-Kandarakis et al., 2009; Raman, 2014; Sharma and Goyal, 2014; Gibbons et al., 2015; Ibrahim et al., 2015) began being observed in multiple vertebrate species at the same time that unprecedented amounts of hormone-disrupting agrichemicals (Raman, 2014; USGS National Water Quality Assessment, 2023) began being applied on multiple crops. Exposure to imidacloprid has been experimentally shown to cause the distinctive birth defects in white-tailed deer (Berheim et al., 2019) that were observed in wild deer in western Montana beginning in spring of 1995, as well as failure to thrive and mortality, as reported in newborn cervids in Wyoming (Smith et al., 2006). Do observations and documentation that profound birth defects began being observed during the spring immediately after the first widespread use of imidacloprid prove that it was responsible? Obviously, it does not, but it strongly suggests that more testing of animals, plants and surface water should be considered, especially following the results of the published experimental study on effects of imidacloprid exposure in white-tailed deer (Berheim et al., 2019).

4.1. Fungicides

Beginning in 1994, the outbreak of late blight in potato fields of nearby Idaho, as well as in eastern Oregon and Washington (Fig. 1), resulted in the tenfold increase in use of fungicides (e.g., Fry and Goodwin, 1997; National Agricultural Research Service, 1998; Henderson et al., 2007; Raman, 2014). Chlorothalonil (2,4,5,6-tetrachlorosophthalonitrile), with trade names Daconil, Bravo and others, is a broad-spectrum fungicide widely used in agriculture, especially by potato, tomato, wheat, and barley growers, and on lawn grass and turf farms (Raman, 2014). This chemical is most toxic when inhaled and has deleterious effects on many organisms and the environment in general (Caux et al., 1996; Raman, 2014, and references therein), in part because the main metabolite is far more toxic and hormone disrupting than the parent fungicide (Zhang et al., 2016).

Cyanide molecules, which chlorothalonil contains, have been shown to be especially damaging to exposed prenatal ruminants (Soto-Blanco and Gorniak, 2004). Symptoms of exposure to organochlorine pesticides, such as chlorothalonil or 2,4-D, include disruption of calcium metabolism and thyroid-hormone function (Jayaraj et al., 2017, and references therein). Chlorothalonil alone is extremely toxic to fish and amphibians at low concentrations, as well as to invertebrates such as insects, earthworms, and microorganisms (Zhang et al., 2016, and references therein). Spray drift and atmospheric deposition of chlorothalonil in rain and snow has been shown to contaminate growing plants and surface waters over extensive areas (Caux et al., 1996; Jayaraj et al., 2017).

In laboratory studies, exposure to chlorothalonil caused loss of embryos in mammals, as well as causing kidney and liver damage, genetic damage, and cancer of the kidneys (Oruc, 2010; Jayaraj et al., 2017).

Damage to the liver and kidneys can interfere with an exposed animal's ability to detoxify and excrete other toxins to which it is exposed. Thus, synergy with other pesticides in the environment likely results in greater injury to the internal organs. For example, unusually high mortality was reported in several vertebrate species in summer and fall of 1994, and multiple previously unreported and uncommon birth defects were found in young animals born in spring of 1995 (Hoy et al., 2002, 2011, 2015; Hoy, 2017). Most importantly, these adverse health issues were observed following the increase in use of chlorothalonil and other fungicides began for the control of potato blight (National Agricultural Research Service, 1998).

4.2. Neonicotinoids

Insect-control measures in agriculture utilize a huge variety of chemicals, many of which disrupt normal cellular functions in exposed vertebrates, with adverse effects on reproduction and neonatal development (e.g., Ngoula et al., 2012; Thompson et al., 2020). Imidacloprid, a neonicotinoid insecticide, was newly registered and began being used in summer of 1994 (Gibbons et al., 2015; USGS National Water Quality Assessment) on fields in Oregon, Washington, and Idaho, directly upwind of Montana and Wyoming, including the Greater Yellowstone region. By 2014, imidacloprid was the most used insecticide throughout the United States and the rest of the world (Gibbons et al., 2015).

Imidacloprid disrupts normal nerve transmission and is more toxic to insects and other invertebrates than to vertebrates because it binds more effectively to the receptors of invertebrate nerve cells (Gibbons et al., 2015, and references therein). Imidacloprid is a systemic insecticide, which means that plants take it up from the soil or through the leaves, and it spreads throughout the plant's stems, leaves, fruit, and flowers. When insects consume treated plants, they ingest the insecticide, which damages their nervous systems, causing mortality (summarized from U. S. National Pesticide Information Center and references therein). Many studies have shown how damaging the highly water-soluble imidacloprid can be to insects, even at very low doses (e.g., Ngoula et al., 2012; Bishop et al., 2018; Thompson et al., 2020). Multiple studies have shown how immune suppression from exposure to neonicotinoids has resulted in outbreaks of infectious diseases in bumblebees, honeybees, and importantly for this review, several vertebrate species (Mason et al., 2013, and references therein).

Despite assumed lower sensitivity in vertebrates, neonicotinoids have been implicated in population declines of small vertebrates [e.g., Mason et al., 2013; Gibbons et al. (2015); Burke et al. (2018); Mikolić and Karačonji (2018); Mineau and Callaghan (2018); Zeid et al. (2018). Indeed, neonicotinoids pose special threats to mammalian hormone systems (Burke et al., 2018; Mikolić and Karačonji, 2018; Berheim et al., 2019). A review by Oakes et al. (2018) examined how nicotine alters the homeostasis of the renin-angiotensin system, which regulates blood pressure, as well as fluid and electrolyte balance in mammals, and thus is important in regulating renal, autonomic, cardiovascular, and pulmonary functions. Recent reviews (e.g., Houchat et al., 2020; Costas-Ferreira and Faro, 2021) have discussed the findings of multiple effects of neonicotinoid insecticides on mammalian cholinergic functions.

Herbivorous mammals are exposed by directly ingesting plants and drinking water containing systemic insecticides such as imidacloprid and other neonicotinoids, causing concentration in the spleen (Berheim et al., 2019). Testing of spleens for imidacloprid in Minnesota white-tailed deer, which began in 2019, reported 94% testing positive for neonicotinoids in 2021 (Hagen, et al., 2019). This extremely high prevalence of exposure in white-tailed deer suggests that other grazing animals, both wild and domestic, would likely test positive for neonicotinoids at similar prevalence. Most concerning for people, a 2022 study of pregnant women found that neonicotinoid insecticides and their metabolites can pass through the human placenta unimpeded, exposing the fetus when the mother is exposed (Zhang et al., 2022). Those toxins very likely can do the same in other pregnant mammals.

Genital malformations and intersex variation can be caused by exposure to anti-androgenic or endocrine-disrupting chemicals, or both simultaneously (Lyons, 2008; Rich et al., 2016; Conley et al., 2018). In their review, Mikolić and Karaconji (2018) concluded that imidacloprid is an endocrine disruptor; exposure can alter essential reproductive functions by affecting hormone levels. As such, it can also cause reproductive organ disruption and suppression of function that may result in infertility. Pre-natal exposure to imidacloprid caused in-utero developmental neurobehavioral deficits that can cause long-term effects lasting into adulthood (see also Burke et al., 2018).

In March 2019, 25 years after imidacloprid was registered for use, a ground-breaking study on captive white-tailed deer was published that clearly demonstrated the effects of imidacloprid on a large mammal species (Berheim et al., 2019). The study showed experimentally that concentrations of imidacloprid detected in the spleens of does (adult female deer) and fawns were directly related to the probability of mortality. Fawns with congenital defects, including underdeveloped jaw bones and reproductive malformations, had higher levels of imidacloprid in their spleens than normal fawns. As imidacloprid levels increased, fawn survival, jaw-bone lengths, body weight and organ weights decreased, including the weights of genital organs of does and fawns. Berheim et al. (2019) also reported higher concentrations of imidacloprid in many of the spleens collected and tested from 367 hunter-harvested and accident-killed North Dakota white-tailed deer (Fig. 1) than in the spleens of their experimentally-exposed deer. From chemical analyses of spleens of white-tailed deer, both does and fawns, Berheim et al. (2019) found that free thyroxine levels and spleen size decreased as imidacloprid concentrations in the spleen increased. These key findings show that, in mammals, the spleen is an important organ for testing neonicotinoid levels. In addition, behavioral observations indicated that imidacloprid levels in the spleens were correlated with decreased activity levels in both does and fawns. Those findings are completely consistent with the decreased activity levels and higher mortality rates reported in the Jackson-area elk calves in the 1997–99 cohort (Smith et al., 2006), three years after imidacloprid began being used on crops in states directly upwind of the elk study area.

4.3. Glyphosate-based herbicides (GBHs)

The phosphonate, N-(phosphonomethyl)glycine, known as glyphosate, is a broad-spectrum, systemic herbicide and crop desiccant, with antibiotic characteristics. Originally patented as a metal chelator, glyphosate binds to the soluble cations of essential minerals such as calcium, iron, manganese, and zinc (Ca^{2+}, Fe^{2+}, Mn^{2+}, Zn^{2+}) in soils, thereby reducing their availability for uptake by plants (Zobiole et al., 2010, and references therein). Glyphosate also was patented as an antibiotic that stimulates populations of oxidant microorganisms and suppresses reducing microorganisms in the soil (Van Bruggen et al., 2018). This activity also decreases the availability of reduced-state ions of micronutrients that are essential to plants (e.g., Eker et al., 2006; Huber, 2007; Johal and Huber, 2009). Lower micronutrient concentrations in plants decreases their availability to grazing animals (Harding, 1999). Glyphosate's antibiotic action also can alter gut microbes, resulting in malnutrition and damage to the immune system, causing affected organisms to be more susceptible to parasites and diseases (e.g., Samsel and Seneff, 2013; Mesnage et al., 2021).

An essential metal ion of concern is Mn^{2+}, which is required for normal growth, development and cellular homeostasis, notably for bone formation, fat and carbohydrate metabolism, and calcium absorption (Tuormaa, 1996; Rondanelli et al., 2021). Manganese deficiency in animals can result in adverse effects including growth alterations, skeletal abnormalities, reproductive defects, ataxia, and impaired lipid and carbohydrate metabolism; Mn^{2+} deficiencies also are associated with neurodegenerative diseases (Bowman et al., 2011; Samsel and Seneff, 2015). Because the major repositories for Mn^{2+} in the cells are the

mitochondria, exposure to GBH can impair mitochondrial function (Peixoto, 2005), which is essential to all metabolic processes, including embryonic development (Silver et al., 2021). Symptoms of manganese deficiency in beef calves include failure to thrive, inability to get up and follow the mother, and underdeveloped facial bones (Staley et al., 1994).

Exposure to GBH has been reported to disrupt development of the head, eyes, and brain by impairing retinoic-acid signaling in vertebrates (Paganelli et al., 2010). Exposure to GBH resulted in multiple changes in uterine development of deliberately exposed postnatal lambs, with adverse consequences for uterine differentiation and functionality (Alarcón et al., 2019, 2020). Ingaramo et al. (2020) reviewed studies on glyphosate and GBH, discussing how exposure to continuous low doses adversely affects the reproductive tracts of female ruminants and acts as an endocrine disrupter to reduce fertility.

Reproductive toxicity as a result of exposure to very low amounts of GBH has been reported in many studies since glyphosate began being used as an herbicide (e.g., Romano et al., 2010, 2012; Jarrell et al., 2020). In a review of GBH formulations and reproductive toxicity in animals, the effects of GBHs and their ingredients on the reproductive health of females across a range of vertebrate species included failure to become pregnant, prenatal mortality, and neonatal abnormalities (Jarrell et al., 2020). Thus, such exposures to GBHs are also consistent with the decrease in Yellowstone-region elk populations and low calf/100 cow ratios documented by Smith et al. (2006) and others, as well as the reported congenital malformations and adverse health effects on ruminants in western Montana (Hoy et al., 2002, 2011, 2015).

In addition to direct effects, Kubsad et al. (2019) showed that a very low, short-term exposure to glyphosate in gestating female rats resulted in transgenerational effects. They documented pathologies in the F2 (grand-offspring) and F3 (great-grand offspring), including prostate disease, obesity, kidney disease, ovarian disease, and parturition (birth) abnormalities. The authors recommended that the generational toxicology of glyphosate be considered in causes of diseases in future generations. In the many generations of animals since those first exposed to glyphosate in the 1970s, with subsequent exposure constantly escalating, generational toxicology and transgenerational effects of glyphosate should be of utmost consideration in protecting the health of all animals, including humans.

4.4. *Combinations of endocrine-disrupting chemicals*

Numerous studies suggest simultaneous exposure to multiple chemicals such as GBH and other heavily used pesticides can adversely disrupt pre- and post-natal cellular processes (e.g., Rolland, 2000; Diamanti-Kandarakis et al., 2009; Gore et al., 2015, and references therein). Such exposure has the potential to induce metabolic disorders by disturbing the physical process of energy absorption in the intestine and energy storage in the liver, adipose tissue and skeletal muscle in humans and other mammals, thereby disrupting energy regulation (He et al., 2020). Thus, GBH and imidacloprid, when working synergistically with other pesticides, additives, or metabolites, can contribute to the disruption of mitochondrial functions [also associated with Mn^{2+} deficiency (see Tuormaa, 1996; Bowman et al., 2011; Rondanelli et al., 2021), discussed previously], resulting in the reduced physical activity observed in exposed animals (e.g., Smith et al., 2006; Berheim et al., 2019).

Pesticide mixtures also can induce congenital defects of reproductive organs. For example, shortened anogenital distance, delayed puberty and extreme genital malformations were found on male rats exposed in utero to doses of a dilute mixture of phthalates and pesticides below which none of the individual chemicals had been shown to produce an effect (Conley et al., 2021). Although chlorothalonil and GBH were used in the region prior to 1995, two male reproductive malformations, underdeveloped penile sheath and misaligned hemiscrota, were first reported on mammals following the registration and extensive use of imidacloprid (Hoy et al., 2002).

Also, regarding birth defects and infertility, GBH and a primary additive, polyethoxylated alkylamines (POEA), disrupted the functions of the Sertoli cell line (TM4) in experimental studies with immature mice (Vanlaeys et al., 2018). Formulations of GBH induced transmembrane (TM4) mitochondrial dysfunction, disruption of cell-detoxification systems, lipid-droplet accumulation, and mortality, even at sub-agricultural exposures. Because Sertoli cells are essential for testicular development and the normal onset of spermatogenesis, disturbance of their function likely contributes to the disruption of reproductive function demonstrated in prepubertal mammals exposed to GBH. Glyphosate and 2,4-D formulations are well known as androgen-active substances that can decrease serum-testosterone concentrations (Romano et al., 2012). Genital malformations and intersex variation can be caused by exposure to anti-androgenic or endocrine-disrupting chemicals, or both simultaneously (Lyons, 2008; Rich et al., 2016; Conley et al., 2018; Mikolić and Karačonji, 2018).

Weather fronts passing over heavily sprayed fields, bare in winter, carry pesticide-laden dust that is deposited over western North America in rain and snow (e.g., Davidson and Knapp, 2007; Hageman et al., 2010; Usenko et al., 2010). Consequently, all organisms downwind of fields with high usage are exposed to toxic mixtures of pesticides that continuously contaminate air, surface water, soil, and foliage. Mixtures of pesticides found in surface waters worldwide are persistent and more toxic than individual compounds, causing adverse effects on non-target organisms at low concentrations (de Souza et al., 2020).

Human newborns are, of course, non-targets of pesticides, but are similarly affected. For example, infants born in major wheat-producing states in the USA suffered significantly higher incidences of circulatory and respiratory malformations in rural counties with high proportions of wheat acreage (Schreinemachers, 2003). Musculoskeletal and integumental anomalies were also elevated in the high wheat-producing counties, as was infant mortality in males from congenital anomalies. Infants conceived during April–June, the time of herbicide application, showed increased risk of such malformations (Schreinemachers, 2003). Highly significant correlations between the increase in glyphosate applications and the increase in 22 human diseases have been documented (Swanson et al., 2014). That paper also reported that the amount of glyphosate applied to crops increased fourfold between 1996 and 1999.

Another study (Gerona et al., 2022) found glyphosate in the urine of 99% of 187 pregnant women; higher maternal glyphosate levels in the first trimester were associated with lower birth weight percentiles and higher neonatal intensive-care unit admissions. This groundbreaking study augments growing research linking glyphosate to birth defects, miscarriage and infertility in animals (e.g., Hoy et al., 2015, and references therein). An interesting comparison is that the Wyoming elk calves born in the 1997–99 study period, especially female calves, had a higher rate of mortality and those that survived took four times as long to become strong enough to join the nurse herd compared with those in the 1990–92 cohort (Smith et al., 2006).

5. Recent fluctuations in yellowstone elk populations

Returning to the elk populations in the northern Yellowstone region, by 2005 counts had declined to approximately 7,000, one third that in 1994 (Smith et al., 2019). Continued decline resulted in a population of <4000 elk in 2014 (Mosley and Mundinger, 2018). Thus, between 1994 and 2014, the resident population decreased by more than 75%, a decline that could not be explained by weather, predation, or human harvest. An average population of 130 wolves over the last 25 years would be unlikely to kill the maximum number of 20–22 elk per wolf per year, since they also eat other prey (Smith et al., 2019). Horne et al. (2019) reported that only 28% of elk-calf mortality was caused by wolves compared to 45% by mountain lions. Predation by grizzly bears was also found to cause higher calf mortality than predation by wolves (Garrott et al., 2009). Malnutrition accounted for 9% of adult-cow

mortality and 10% for calves, with smaller calves and older cows being preferentially selected by the wolves. Of 29 elk directly observed to have been killed by wolves, 9 were calves and 20 were older individuals (Smith et al., 2019). If the elk population had continued to have the 1990–92 survival rates of calves, especially female calves, the northern Yellowstone elk population should have remained relatively stable at ~10,000 elk, despite natural predation and the park's difficult winters.

In 2015, the resident Yellowstone elk population began recovering and by 2018 exceeded 7,500, although calf production remained below 20 juveniles/100 cows in 2018 and 2019 (National Park Service News Release, 2019, National Park Service). As of January 2023, there were 108 wolves in 9 packs living in Yellowstone, though Treves and Santiago-Avila (2023, and references therein) suggested that recent laws in adjoining states allowing wolf-killing could have serious consequences for the viability of wolf populations in the region.

A declining prevalence of underbite (brachygnathia superior) has been documented since 2014 on hunter-harvested elk, white-tailed deer and other wild ruminants from Montana (Table 1). The average incidences of underbite of 30% for adult elk and 48% for adult white-tailed deer during the period from 2012 to 2015, declined to 4% on elk and 16% on white-tailed deer in 2021–2022. Mule-deer underbite prevalence declined from a high of 73% in 2012–2015, to 27% in 2021–2022. Beginning in 2014 and continuing through at least 2018, the sex ratio on accident-killed white-tailed deer fawns was significantly skewed in favor of females, averaging 35 M to 65F/100 fawns (Stone et al., 2019). Why the prevalence of underbite declined and the sex ratio began to favor females remains unknown. An increase in female ruminants, in addition to fewer or less severe birth defects, would likely result in higher numbers of viable young.

Considering the trend of declining severity of birth defects after two decades (1994–2014), in the context of genetic responses in wildlife populations elsewhere in the world, generates an interesting question. Could environmental conditions that strongly selected against females most sensitive to endocrine disruption result in altered populations less sensitive to endocrine disruption, especially in females? One example of rapid selection in recent decades is the remarkable increase in tuskless female elephants in Mozambique (Poole and Granli, 2022; Campbell--Staton et al., 2021) in response to 15 years of intense ivory poaching. Other examples include genetic changes in feral dogs and other species exposed to radiation in the area around Chernobyl after 25 years (Spatola et al., 2023). One possible clue in the case of birth defects in ruminants is the change in sex ratios from favoring males to favoring females. Endocrine disruption that weakens mostly female neonates would strongly select for females least susceptible. Endocrine disruption that renders some proportion of males sterile might have less impact on sex ratios initially, as there are generally excess males in a ruminant population. Ultimately, however, selection for fertile males should also emerge.

6. Human-altered ecosystems

After spending years in the Yellowstone ecosystem trying to find causes for the decline in the elk population, Middleton et al. (2013) concluded that no single factor could explain the decline. In 2014, Middleton told a reporter, "The elk population in Yellowstone is at the mercy of a much larger, human-altered ecosystem" (Wilcox, 2014, p. 6).

Among the factors associated with "human-altered ecosystems" are frequently changing exposures to multiple agrichemicals (Hoy et al., 2015; Berheim et al., 2019). Plants directly uptake systemic herbicides and insecticides into the foliage that ruminants consume (e.g., Klich et al., 2020). Contaminated foliage ingested by grazing animals has resulted in measurable levels of pesticides in their organs (e.g., Berheim et al., 2019), especially the most used insecticide, imidacloprid, which has been experimentally shown to induce birth defects and mortality in white-tailed deer.

Analogous "issues" associated with endocrine disruption by anthropogenically produced chemicals have been recognized and reported many times over the past 75 years. The harmful effects of exposure to cyanide-based and organophosphate pesticides have been known for decades. Rachel Carson (1962) warned the world about the consequences of endocrine-disrupting pesticides in her book *Silent Spring*, for example, citing studies of chemical caponization of roosters. Colborn et al. (1996) described in detail how hormone-disrupting chemicals impact reproduction in both humans and wildlife in *Our Stolen Future*. Numerous more recent reviews (e.g., Krimsky, 2000; Mason et al., 2013; Lushchak et al., 2018; Sonne et al., 2020; Thompson et al., 2020; many more) have further revealed the serious long-term effects of low doses of teratogenic agrichemicals on non-target organisms, including humans (e.g., Gray, 1992; Colborn et al., 1993; Schreinemachers, 2003; Hoy et al., 2015; Gerona et al., 2022; many more).

For individuals who have worked closely with domestic animals and wildlife for many decades, birth defects such as facial and reproductive deformities are readily apparent (e.g., Hoy, 2017; Berheim et al., 2019). Why have these anomalies not been more widely recognized in the nearly three decades since they began? Most likely, the statement attributed to Nobel Laureate Albert Szent-Györgyi (1972): "Discovery is seeing what everybody else has seen and thinking what nobody else has thought" seems to apply here. Wildlife biologists in Yellowstone National Park certainly have seen bull bison that have little or no visible scrotum, but either never noticed or, if they did, never thought to ask "Why?"

Unfortunately for the affected wildlife, unless quite severe, underbite is visually subtle (Appendices Ab, Ae, Bc) and has been largely overlooked, as have male reproductive malformations. Most individuals, even researchers, likely do not recognize the conditions as being congenital malformations. In the ecological realm, such phenomena are known as "Shifting Baselines" (e.g., McHarg, 1992; Pauly, 1995; Papworth et al., 2009). Modern farmers and ranchers may notice facial abnormalities, weak bones, and undescended testicles in their livestock, but not realize that such features were rarely seen a half-century ago. In addition, the tendency to consider birth defects in livestock and wildlife to be genetic, or as some deficiency in agricultural husbandry, reduces the probability that such abnormalities will be reported, let alone considered to be environmentally induced.

The primary purpose of this paper is to ask specific questions about the possibility that, beginning in 1994, the explosive increase in use of certain agrichemicals, which are now widely recognized as teratogenic, impacted wildlife in western states of the US. In doing so, we have provided both published evidence and new data that multiple ruminant species experienced specific health conditions and population declines that appear to be consistent with teratogenic exposures. Our recommendations are to consider these possibilities for domestic animals and wildlife. We further recommend that wild ruminants captured alive or examined dead, be checked for facial anomalies such as underbite, overbite, and other craniofacial defects. Male mammals similarly available for inspection should be examined for external reproductive malformations, including ectopic testicles, misaligned, short, or absent hemiscrota, and an abnormally short penile sheath on species with that organ (e.g., deer and rodents). Additional studies of the effects of exposure to agrichemicals, especially the most heavily used, well-known, teratogenic pesticides, including neonicotinoids such as imidacloprid, fungicides such as chlorothalonil, and glyphosate-based herbicides, any two of those, or all simultaneously, on ruminant species could indicate if increased exposure to those pesticides might contribute to declines in ruminant populations, both wild and domestic. When experimental studies of live ruminants are undertaken, we further suggest that domestic livestock such as goats are far easier and more humane to work with than wildlife.

7. Conclusions

The discovery of reproductive and craniofacial abnormalities in

white-tailed deer fawns born in western Montana in spring 1995, and quantitative documentation thereof; observations and work with other wildlife and domestic animals in which especially craniofacial abnormalities quite abruptly became common, including birds with abnormally short upper bills; and regularly visiting Yellowstone National Park each spring and autumn and noting that some bull bison had anomalously small scrotums; stimulated the question "What is causing these malformations and why did they appear in the mid-1990s?" The coincidental release of wolves into Yellowstone Park in 1995 and 1996, followed by the subsequent decline of elk populations and widespread public assumption that wolves were to blame, generated the question: "Might wildlife in the Yellowstone region be experiencing abnormalities that contributed to population declines?" That question led to research into publications and technical reports, especially multi-year studies, on wildlife in the Greater Yellowstone region.

In researching and publishing on the reproductive and craniofacial abnormalities, the issue of endocrine disruption naturally emerged, along with the question "What happened in the mid-1990s that could have resulted in substantial increases in regional exposures to endocrine disruptors in wildlife populations?" That question led to reports of massive increases in regional use of three teratogenic agrichemicals in the mid-1990s.

In this review, we explored the following questions: a) Were massive increases in regional use of teratogenic agrichemicals in the mid-1990s associated with the onset of craniofacial and genital malformations in white-tailed deer and other wild ruminants beginning in 1995? b) Might massive increases in exposure to such chemicals starting in the mid-1990s have contributed to documented declines in vitality and survival of juvenile elk in the greater Yellowstone region between the early and late 1990s?

Exposures to endocrine- and metabolic-disrupting agrichemicals are known to cause congenital fetal hypothyroidism, birth defects, abnormally weak newborns, and other health issues, with consequent increase in mortality in both juveniles and adults. Specifically, experiments with white-tailed deer found that, as imidacloprid levels increased, fawn survival, jawbone lengths, body weight and organ weights decreased, including the weights of genital organs of does and fawns.

Imidacloprid has been found to concentrate in the spleen of an exposed mammal. A straightforward way to investigate the prevalence of exposure is to collect and test spleens of hunter-harvested and accident-killed wildlife, including both predator and prey animals, as well as spleens from slaughtered domestic animals. Craniofacial abnormalities and malformations of male genitalia could be reliably recorded at hunting-management check stations by personnel trained to recognize and document such abnormalities.

If exposure to teratogenic agrichemicals was one factor in regional declines in wild ruminants between 1994 and 2014, are increasing amounts of those same teratogenic substances in the air, water, soil, and on plants still contributing to birth defects and mortality in vertebrates? If so, even if selection occurs in wildlife for genotypes most resistant to endocrine disruption, the effects of ubiquitous teratogens on the health of domestic ruminants and other animals, including humans, will likely continue and possibly accelerate.

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CRediT authorship contribution statement

Judith A. Hoy: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gary T. Haas:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Pamela Hallock:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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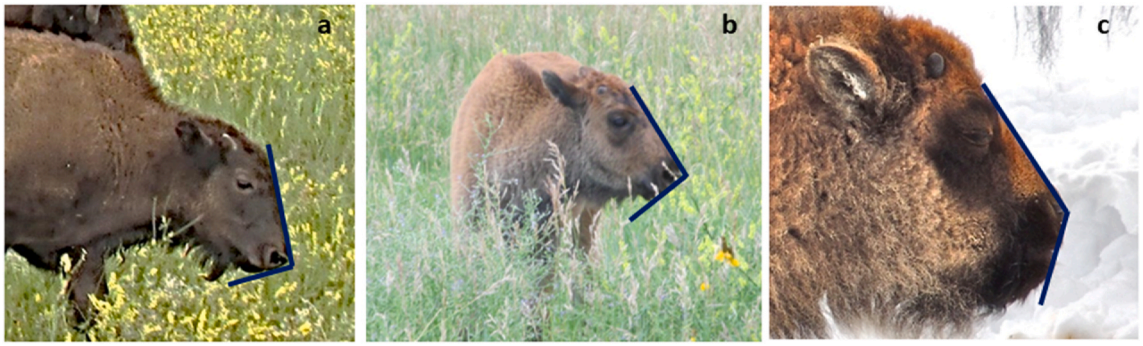
Appendix A. Facial features, including malocclusion types, in two species of Cervidae photographed live: a–c) *Odocoileus virginianus* (white-tailed deer) and d–f) *Cervus canadensis* (elk). a, d) normal bite (the anterior of the lower lip is touching the posterior of the upper lip, indicating that the incisors meet the dental pad); b, e) brachygnathia superior (underbite) occurs when the lower jaw is normal in length and the premaxillary bone is underdeveloped, so the incisors extend forward of the dental pad (see also Fig. 5c, f) brachygnathia inferior (overbite) occurs when the lower jaw is underdeveloped and shorter than normal. Note that underbite is less likely to be recognized by the casual observer, but is more likely to impact nutrition because mothers may not tolerate nursing and, if the affected calf survives to feed on vegetation, grazing is less efficient because the incisors don't meet the dental pad

Appendix B. Bison calves (Bison bison): a, b) calves with normal facial development with superimposed lines illustrating the near-90° angle between face and the base of the nosepad/mouth; c) bison calf with short, underdeveloped upper facial bones with lines illustrating that the angle between the face and nosepad/mouth is ~135°



References

Alarcón, R., Rivera, O.E., Ingaramo, P.I., Rivera, O.E., Dioguardi, G.H., Repetti, M.R., Demonte, L.D., Milesi, M., Varayoud, J., Muñoz-de-Toro, M., Luque, E.H., 2019. Neonatal exposure to a glyphosate-based herbicide alters the histofunctional differentiation of the ovaries and uterus in lambs. Mol. Cell. Endocrinol. 482, 45–56. https://doi:10.1016/j.mce.2018.12.007.

Alarcón, R., Rivera, O.E., Ingaramo, P.I., Tschopp, M.V., Dioguardi, G.H., Milesi, M., Muñoz-de-Toro, M., Luque, E.H., 2020. Neonatal exposure to a glyphosate-based

herbicide alters the uterine differentiation of prepubertal Ewe lambs. Environ. Pollut. 265, 114874. https://doi:10.1016/j.envpol.2020.114874.
Allen, A.L., 1995. Hyperplasia of the thyroid gland and musculoskeletal deformities in two equine abortuses. Can. Vet. J. 36, 34–236. PMid:7600514.
Allen, A.L., Fretz, P.B., Card, C.E., Doige, C.E., 1998. The effects of partial thyroidectomy on the development of the equine fetus. Equine Vet. J. 30, 53–59. https://doi:10.1111/j.2042-3306.1998.tb04088.x.
Barber-Meyer, S.M., Mech, L.D., White, P.J., 2008. Elk calf survival and mortality following wolf restoration to Yellowstone National Park. Wildl. Monogr. 196, 1–30. https://doi:10.2193/2008-004.
Barrett, M.W., Chalmers, G.A., 1975. Congenital anomalies in a neonatal white-tailed deer in Alberta. J. Wildlife. Dis. 11, 497–501. https://doi:10.7589/0090-3558-11.4.497.
Benbrook, C.M., 2012. Impacts of genetically engineered crops on pesticide use in the U. S.–the first sixteen years. Environ. Sci. Eur. 24, 24. https://doi.org/10.1186/2190-4715-24-24.
Berheim, E.H., Jenks, J.A., Lundgren, J.G., Michel, E.S., Grove, D., Jensen, W.F., 2019. Effects of neonicotinoid insecticides on physiology and reproductive characteristics of captive female and fawn white-tailed deer. Sci. Rep. 9, 4534. https://doi:10.1038/s41598-019-40994-9.
Bishop, C.A., Moran, A.J., Toshack, M.C., Elle, E., Maisonneuve, F., Elliott, J.E., 2018. Hummingbirds and bumble bees exposed to neonicotinoid and organophosphate insecticides in the Fraser Valley, British Columbia, Canada. Environ. Toxicol. Chem. 37, 2143–2152. https://doi:10.1002/etc.4174.
Bowman, A.B., Kwakye, G.F., Herrero Hernández, E., Aschner, M., 2011. Role of manganese in neurodegenerative diseases. J. Trace Elem. Med. Biol. 25, 191–203. https://doi:10.1016/j.jtemb.2011.08.144.
Boyce, M.S., 2018. Wolves for Yellowstone: dynamics in time and space. J. Mammal. 99, 1021–1031. https://doi.org/10.1093/jmammal/gyy115.
Bretveld, R.W., Thomas, C.M., Scheepers, P.T., Zielhuis, G.A., Roeleveld, N., 2006. Pesticide exposure: the hormonal function of the female reproductive system disrupted? Reprod. Biol. Endocrinol. 4, 30. https://doi.org/10.1186/1477-7827-4-30.
Brimeyer, D.G., Thomas, T.P., 2004. History of moose management in Wyoming and recent trends in Jackson Hole. Alces 40, 133–144. https://alcesjournal.org/index.php/alces/article/view/447.
Burke, A.P., Niibori, Y., Terayama, H., Ito, M., Pidgeon, C., Arsenault, J., Camareo, P.R., Cummins, C.L., Mateo, R., Sakabe, K., Hampson, D.R., 2018. Mammalian susceptibility to a neonicotinoid insecticide after fetal and early postnatal exposure. Sci. Rep. 8, 16639 https://doi.org/10.1038/s41598-018-35129-5.
Campbell-Staton, S.C., Arnold, B.J., Goncalves, D., Granli, P., Poole, J., Long, R.A., Pringle, R.M., 2021. Ivory poaching and the rapid evolution of tusklessness in African elephants. Science 374, 483–487. https://doi:10.1126/science.abe7389.
Carson, R., 1962. Silent Spring. Houghton Mifflin, New York.
Carstensen, M., Arnold, B.J., Goncalves, D., Granli, P., Poole, J., Long, R.A., Pringle, R. M., 2009. Survival, birth characteristics, and cause-specific mortality of white-tailed deer neonates. J. Wildlife Manage. 73, 175–183. https://doi:10-2193/2006-107.
Caux, P.-Y., Kent, R.A., Fan, G.T., Stephenson, G.L., 1996. Environmental fate and effects of chlorothalonil: a Canadian perspective. Crit.Rev. Env. Sci.Tech. 26, 45–93. https://doi.org/10.1080/10643389609388486.
Cerrizuela, S., Vega-Lopez, G.A., Aybar, M.J., 2020. The role of teratogens in neural crest development. Birth Defects Res 112, 584–632. https://doi:10.1002/bdr2.1644.
Christianson, D., Creel, S., 2014. Ecosystem scale declines in elk recruitment and population growth with wolf colonization: a before-after-control-impact approach. PLoS One 9 (7), e102330. https://doi:10.1371/journal.pone.0102330.
Colborn, T., vom Saal, F.S., Soto, A.M., 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ. Health Perspect. 101, 378–384. https://doi.org/10.1289/ehp.93101378.
Colborn, T., Myers, J.P., Dumanoski, D., 1996. Our Stolen Future: How We Are Threatening Our Fertility, Intelligence, and Survival: A Scientific Detective Story. Dutton, New York, 9780452274143.
Conley, J.M., Lambright, C.S., Evans, N., Cardon, M., Furr, J., Wilson, V., Gray, E., 2018. Mixed "antiandrogenic" chemicals at low individual doses produce reproductive tract malformations in the male rat. Toxicol. Sci. 164, 166–178. https://doi:10.1093/toxsci/kfy069.
Conley, J.M., Lambright, C.S., Evans, N., Cardon, M., Medlock-Kakaley, E., Wilson, V.S., Gray, E., 2021. A mixture of 15 phthalates and pesticides below individual chemical no observed adverse effect levels (NOAELs) produces reproductive tract malformations in the male rat. Environ. Internat. 156, 106615 https://doi.org/10.1016/j.envint.2021.106615.
Costas-Ferreira, C., Faro, L.R.F., 2021. Neurotoxic effects of neonicotinoids on mammals: what is there beyond the activation of nicotinic acetylcholine receptors? A systematic review. Int. J. Mol. Sci. 22, 8413. https://doi.org/10.3390/ijms22168413.
Creel, S., Christianson, D., Liley, S., Winnie Jr., J.A., 2007. Predation risk affects reproductive physiology and demography of elk. Science 315 (5814), 960. https://doi:10.1126/science.1135918.
Davidson, C., Knapp, R.A., 2007. Multiple stressors and amphibian declines: Dual impacts of pesticides and fish on yellow-legged frogs. Ecol. Appl. 17, 587–597. https://doi.org/10.1890/06-0181.
de Souza, R.M., Seibert, D., Quesada, H.B., de Jesus Bassetti, F., Fagundes-Klen, R., Bergamasco, R., 2020. Occurrence, impacts and general aspects of pesticides in surface water: a review. Process Saf. Environ. 135, 22–37. https://doi:10.1016/j.psep.2019.12.035.
Diamanti-Kandarakis, E., Bourguignon, J.-P., Giudice, L.C., Hauser, R., Prins, G.S., Soto, A.M., Zoeller, R.T., Gore, A.C., 2009. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr. Rev. 30, 293–342. https://doi:10.1210/er.2009-0002.
Eberhardt, L.L., White, P.J., Garrott, R.A., Houston, D.B., 2010. A seventy-year history of trends in Yellowstone's northern elk herd. J. Wildlife Manage. 71, 594–602. https://doi:10.2193/2005-770.
Ellenberger, J.H., Byrne, A.E., 2015. Population status and trends of big game and greater sage grouse in southeast Montana and northeast Wyoming. https://www.nwf.org/~/media/PDFs/Media%20Center%20-%20Press%20Releases/11-17-15-MT-WY-Wildlife-Report-Final.pdf.
Eker, S., Ozturk, L., Yazici, A., Erenoglu, B., Romheld, V., Cakmak, I., 2006. Foliar-applied glyphosate substantially reduced uptake and transport of iron and manganese in sunflower (*Helianthus annuus* L.) plants. J. Agric. Food Chem. 54, 10019–10025. https://doi:10.1021/jf0625196.
Enk, T.A., Picton, H.O., Williams, J.S., 2001. Factors limiting bighorn sheep population in Montana following a dieoff. Northwest Sci. 75, 280–291. https://hdl.handle.net/2376/945.
Fischer, H., 1995. Wolf wars: the remarkable inside story of the restoration of wolves to Yellowstone. Helena, MT: Falcon Guides 183, 1560443529.
Fry, W.E., Goodwin, S.B., 1997. Re-emergence of potato and tomato Late Blight in the United States. Plant Dis. 81, 1349–1357. https://doi:10.1094/PDIS.1997.81.12.1349.
Garrott, R., White, P.J., Rotella, J., 2009. The Madison headwaters elk herd: transitioning from bottom-up regulation to top-down limitation. In: Garrot, R., et al. (Eds.), The Ecology of Large Mammals in Central Yellowstone: Sixteen Years of Integrated Field Studies, vol. 3. Terrestrial Ecology Series, pp. 489–517. https://doi:10.1016/S1936-7961(08)00223-6.
Gerona, R.R., Reiter, J.L., Zakharevich, I., Proctor, C., Ying, J., Mesnage, R., Antoniou, M., Winchester, P.D., 2022. Glyphosate exposure in early pregnancy and reduced fetal growth: a prospective observational study of high-risk pregnancies. Environ. Health. 21, 95. https://doi.org/10.1186/s12940-022-00906-3.
Gibbons, D., Morrissey, C., Mineau, P., 2015. A review of the direct and indirect effects of neonicotinoids and fipronil on vertebrate wildlife. Environ. Sci. Pollut. Res. 22, 103–118. https://doi.org/10.1007/s11356-014-3180.
Gore, A.C., Chappell, V.A., Fenton, S.E., Flaws, J.A., Nadal, A., Prins, G.S., Toppari, J., Zoeller, R.T., 2015. Executive summary to EDC-2: the endocrine society's second scientific statement on endocrine-disrupting chemicals, 2015 Dec Endocr. Rev. 36 (6), 593–602. https://doi.org/10.1210/er.2015-1093. Epub 2015 Sep 28. PMID: 26414233; PMCID: PMC4702495.
Gray, L.E., 1992. Chemical-induced alterations of sexual differentiation: a review of effects in humans and rodents. In: Colborn, T., Clement, C. (Eds.), Chemically Induced Alterations in Sexual and Functional Development: the Wildlife/Human Connection, Adv, vol. 21. Mod. Env., p. 203, 0911131353.
Griffin, K.A., Hebblewhite, M., Robinson, H.S., Zager, P., Barber-Meyer, S.M., Christianson, D., Creel, S., Harris, N.C., Hurley, M.A., Jackson, DeW.H., Johnson, B. K., Myers, W.L., Raithel, J.D., Shlegel, M., Smith, B.L., White, C., White, P.J., 2011. Neonatal mortality of elk driven by climate, predator phenology and predator community composition. J. Anim. Ecol. 80, 1246–1257. https://doi:10.1111/j.1365-2656.2011.01856.x.
Guillette Jr., L.J., Guillette, E.A., 1996. Environmental contaminants and reproductive abnormalities in wildlife: implications for public health? Toxicol. Industrial Health 12, 537–550. https://doi.org/10.1177/07482337960120032.
Hageman, K.J., Hafner, W.D., Campbell, D.H., Jaffe, D.A., Landers, D.H., Massey Simonic, S.L., 2010. Variability in pesticide deposition and source contributions to snowpack in western U.S. National Parks. Environ. Sci. Technol. 44, 4452–4458. https://doi:org.ezproxy.lib.usf.edu/10.1021/es100290q.
Hagen, P., Carstensen, M., Michel, E., Kelly, J., 2019. Assessing Neonicotinoids Exposure in Free-Ranging White-tailed Deer in Minnesota. Minnesota Department of Natural Resourses. https://files.dnr.state.mn.us/wildlife/research/summaries/2019/ungulates/2019ug001.pdf.
Hamilton, T.R.D., Mendes, C.M., de Castro, L.S., de Assis, P.M., Siqueira, A.F.P., Delgado, J.D., Goissis, M.D., Muiño-Blanco, T., Cebrián-Pérez, J.A., Nichi, M., Visintin, J.A., Assumpcao, M.E.O.D., 2016. Evaluation of lasting effects of heat stress on sperm profile and oxidative status of ram semen and epididymal sperm. Oxid. Med. Cell. Longev. 2016 https://doi.org/10.1155/2016/1687657. Art. ID. 1687657.
Handel, C.M., van Hemert, C., 2015. Environmental contaminants and chromosomal damage associated with beak deformities in a resident North American passerine. Environ. Toxicol. Chem. 34, 314–327. https://doi:10.1002/etc.2799.
Handel, C.M., Pajot, L.M., Matsuoka, S.M., Van Hemert, C., Terenzi, J., Talbot, S.L., Mulcahy, D.M., Meteyer, C.U., Trust, K.A., 2010. Epizootic of beak deformities among wild birds in Alaska: an emerging disease in North America? The Auk 127, 882–898. https://doi:10.1525/auk.2010.10111.
Hansen, S., 2020. Range-wide status of black-tailed and mule deer. Mule Deer Working Group. Western Association of Fish and Wildlife Agencies 44. https://wafwa.org/wp-content/uploads/2020/08/2020_MuleDeer-and-BTD_Status-Update.pdf.
Harding, J., 1999. Nutritional causes of impaired fetal growth and their treatment. J. R. Soc. Med. 92, 612–615. https://doi:10.1177/014107689909201202.
He, B., Ni, Y., Jin, Y., Fu, Z., 2020. Pesticide-induced energy metabolic disorders. Sci. Total Environ. 29, 139033. https://doi:10.1016/j.scitotenv.2020.139033.
Henderson, D., Williams, C.J., Miller, J.S., 2007. Forecasting late blight in potato crops of southern Idaho using logistic regression analysis. Plant Dis. 91, 951–956. https://doi.org/10.1094/PDIS-91-8-0951.
Horne, J.S., Hurley, M.A., White, C.G., Rachael, J., 2019. Effects of wolf pack size and winter conditions on elk mortality. J. Wildlife Manage. 83, 1103–1116. https://doi.org/10.1002/jwmg.21689.
Houchat, J.N., Cartereau, A., Le Mauff, A., Taillebois, E., Thany, S.H., 2020. An overview on the effect of neonicotinoid insecticides on mammalian cholinergic functions

through the activation of neuronal nicotinic acetylcholine receptors. Int. J. Environ. Res. 17, E3222. https://doi:10.3390/ijerph17093222.
Hoy, J.A., Hoy, R.D., Seba, D., Kerstetter, T.H., 2002. Genital abnormalities in white-tailed deer (*Odocoileus virginianus*) in west-central Montana: pesticide exposure as a possible cause. J. Environ. Biol. 23, 189–197. PMID: 12602857.
Hoy, J.A., Haas, G.T., Hoy, R.D., Hallock, P., 2011. Observations of brachygnathia superior in wild ruminants in western Montana, USA. Wildl.Biol. Pract. 7, 15–29. https://doi.org/10.2461/wbp.2011.7.13.
Hoy, J.A., Swanson, N., Seneff, S., 2015. The high cost of pesticides: human and animal diseases. Poult. Fish Wildl. Sci. 3, 1000132. https://doi:10.4172/2375-446X.1000132.
Hoy, J.A., 2017. Changing faces: the consequences of exposure to gene and thyroid disrupting toxins. CreateSpace Publ. 1–314. ISBN-10: 1979134804.
Huber, D.M., 2007. Strategies to ameliorate glyphosate immobilization of Mn and its impact on disease. Phytopathology 97, S168. https://doi.org/10.1094/PHYTO.2007.97.7.S166.
Hutto, J., 2013. Touching the Wild: Living with the Mule Deer of Deadman Gulch. Skyhorse. Simon & Schuster, New York. -13: 9781628735536.
Ibrahim, K.A., El-Desouky, M.A., Abou-Yousef, H.M., Gabrowny, K.H., El-Sayed, A.S., 2015. Imidacloprid and/or Esfenvalerate induce apoptosis and disrupt thyroid hormones in neonatal rats. GJBBR 10, 106–112. https://doi:10.5829/idosi.gjbb.2015.10.03.1121.
Ingaramo, P., Alarcón, R., Muñoz-de-Toro, M., Luque, E.H., 2020. Are glyphosate and glyphosate-based herbicides endocrine disruptors that alter female fertility? Mol. Cell Endocrin. 10, 110934. https://doi:10.1016/j.mce.2020.110934.
Jarrell, Z.R., Ahammad, M.U., Benson, A.P., 2020. Glyphosate-based herbicide formulations and reproductive toxicity in animals. Vet. Anim. Sci. 10, 100126. https://doi:10.1016/j.vas.2020.100126.
Jayaraj, R., Megha, P., Sreedev, P., 2017. Organochlorine pesticides, their toxic effects on living organisms and their fate in the environment. Interdiscip. Toxicol. 9, 90–100. https://doi:10.1515/intox-2016-0012.
Johal, G.S., Huber, D.M., 2009. Glyphosate effects on diseases of plants. Europ. J. Agron. 31, 144–152. https://doi.org/10.1016/j.eja.2009.04.004.
Kapoor, U., Srivastava, M.K., Srivastava, L.P., 2011. Toxicological impact of technical imidacloprid on ovarian morphology, hormones and antioxidant enzymes in female rats. Food Chem. Toxicol. 49, 3086–3089. https://doi:10.1016/j.fct.2011.09.009.
Kissell Jr., R.E., Irby, L.R., Mackie, R.J., 1996. Competitive Interactions Among Bighorn Sheep, Feral Horses, and Mule Deer in Bighorn Canyon National Recreation Area and Pryor Mountain Wild Horse Range: Bozeman. Montana State University, p. 146. Final report on Cooperative Agreement CA-1268-9017.
Klich, D., Lopucki, R., Stachniuk, A., Sporek, M., Fornal, E., Wojciechowska, M., Olech, W., 2020. Pesticides and conservation of large ungulates: health risk to European bison from plant protection products as a result of crop depredation. PLoS One 15, e0228243. https://doi.org/10.1371/journal.pone.0228243.
Koeth, C., 2008. Clinging to Existence. Montana Outdoors Sept-Oct, pp. 22–27. https://issuu.com/montanaoutdoors/docs/so08.
Kraabel, B.J., Miller, M.W., 1997. Effect of simulated stress on the susceptibility of bighorn sheep neutrophils to *Pasteurella haemolytica* leukotoxin. J. Wildl. Dis. 33, 558–566. https://doi:10.7589/0090-3558-33.3.558.
Krimsky, S., 2000. Hormonal chaos: the scientific and social origins of the environmental endocrine hypothesis. BMJ Publishers 321 (7259), 516. PMCID: PMC1118410.
Kubsad, D., Nilsson, E.E., King, S.E., Sadler-Riggleman, I., Beck, D., Skinner, M.K., 2019. Assessment of glyphosate-induced epigenetic transgenerational inheritance of pathologies and sperm epimutations: generational toxicology. Sci. Rep. 9, 6372 https://doi.org/10.l038/s41598-019-42860-0.
Leemans, M., Couderq, S., Demeneix, B., Fini, J.-B., 2019. Pesticides with potential thyroid hormone-disrupting effects: a review of recent data. Front. Endocrinol. 10, 743. https://doi.org/10.3389/fendo.2019.00743.
Lushchak, V.I., Matviishyn, T.M., Husak, V.V., Storey, J.M., Storey, K.B., 2018. Pesticide toxicity: a mechanistic approach. EXCLI J 17, 1101–1136. https://doi.org/10.17179/excli2018-1710.
Lyons, G., 2008. Effects of Pollutants on the Reproductive Health of Male Vertebrate Wildlife-Males under Threat. CHEMTrust. www.chemtrust.org.uk.
MacNulty, D.R., Stahler, D.R., Wyman, C.T., Ruprecht, J., Smith, D.W., 2016. The challenge of understanding northern Yellowstone elk dynamics after wolf reintroduction. Yellowstone Science 24, 25–33. https://www.nps.gov/yell/learn/ys-24-1-the-challenge-of-understanding-northern-yellowstone-elk-dynamics-after-wolf-reintroduction.htm.
Mason, R., Tennekes, Sánchez-Bayo, F., Jepsen, P.U., 2013. Immune suppression by neonictinoid insecticides at the root of global wildlife declines. J. Enviro. Immunol. Toxicol. 1, 3–13. https://doi:10.7178/jeit.1.
McHarg, I.L., 1992. Design with Nature, 25th Anniversary Edition. Wiley, New York, NY, 047111460X.
Mech, L.D., 2007. Femur-marrow fat of white-tailed deer fawns killed by wolves. J. Wildlife Manage. 71, 920–923. https://doi:10-2193/2006-153.
Mesnage, R., Teixeira, M., Mandrioli, D., Falcioni, L., Ducarmon, Q.R., Zwittink, R.D., Mazzacuva, F., Caldwell, A., Halket, J., Amiel, C., Panoff, J.-M., Belpoggi, F., Antoniou, M.N., 2021. Use of shotgun metagenomics and metabolomics to evaluate the impact of glyphosate or Roundup Mon 52276 on the gut microbiota and serum metabolome of Sprague-Dawley rats. Environ. Health Persp. 129 (1), 017005 https://doi.org/10.1289/EHP6990.
Middleton, A.D., Kauffman, M.J., McWhirter, D.E., Cook, J.G., Cook, R.C., Nelson, A.A., Jimenez, M.D., Klaver, R.W., 2013. Animal migration amid shifting patterns of phenology and predation: lessons from a Yellowstone elk herd. Ecology 94, 1245–1256. https://doi.org/10.1890/11-2298.1.
Mikolić, A., Karačonji, I.B., 2018. Imidacloprid as reproductive toxicant and endocrine disruptor: investigations in laboratory animals. Arh. Hig. Rada. Toksikol. 69, 103–108. https://doi.org/10.2478/aiht-2018-69-3144.
Mineau, P., Callaghan, C., 2018. Neonicotinoid Insecticides and Bats and Assessment of the Direct and Indirect Risks. Canadian Wildlife Federation, p. 87. https://cwf-fcf.org/en/resources/research-papers/1809-014-Bats-and-Neonics-Report-high_rez.pdf.
Mosley, J.C., Mundinger, J.G., 2018. History and status of wild ungulate populations on the northern Yellowstone Range. Rangelands 40, 177–188. https://doi.org/10.1016/j.rala.2018.10.006.
Nadeau, M.S., DeCesare, N.J., Brimeyer, D.G., Bergman, E.J., Harris, R.B., Hersey, K.R., Huebner, K.K., Matthews, P.E., Thomas, T.P., 2017. Status and trends of moose populations and hunting opportunity in the western United States. Alces 53, 99–112. https://alcesjournal.org/index.php/alces/article/view/182.
National Agricultural Research Service, 1998. Agricultural chemical usage: 1997 field crops summary. United States Department of Agriculture 1, 1–98. Ag Ch. downloads.usda.library.cornell.edu/usda-esmis/files/2n49t1699/d791sj79d/79408067 1/AgriChemUsFC-05-20-1998.pdf.
National Park Service News Release, 2019. April 4. https://www.nps.gov/yell/learn/news/2019-late-winter-survey-of-northern-yellowstone-elk.htm.
National Park Service. Gray wolf website. https://www.nps.gov/yell/learn/nature/wolves.htm. (Accessed 18 February 2024).
Ngoula, F., Ngouateu, O.B., Kana, J.R., Defang, H.F., Watcho, P., Kamtchouing, P., Tchoumboue, J., 2012. Reproductive and developmental toxicity of insecticides. In: Perveen, F.F. (Ed.), Insecticides: Advances in Integrated Pest Management, vol. 9. Intech Open, Rijeka, pp. 429–456, 978-953-307-780-2. https://doi:10.5772/29153.
Oakes, J.M., Fuchs, R.M., Gardner, J.D., Lazartiques, E., Yue, X., 2018. Nicotine and the renin-angiotensin system. Am. J. Physiol. Regul. Integr. Comp. Physiol. 315, R895–R906. https://doi:10.1152/ajpregu.00099.2018.
O'Gara, B., 1992. Preliminary report on field collections of white-tailed deer on the Lee Metcalf National Refuge. Stevensville (MT): Lee Metcalf National Wildlife Refuge 1–30.
Oruc, H.H., 2010. Fungicides and their effects on animals. In: Carisse, O. (Ed.), Fungicides, vol. 17. InTech Open, Rijeka, pp. 349–362, 978-953-307-266-1.
Paganelli, A., Gnazzo, V., Acosta, H., Lopez, S.L., Carrasco, A.E., 2010. Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signaling. Chem. Res. Toxicol. 23, 1586–1595. https://doi.org/10.1021/tx1001749.
Papworth, S.K., Rist, J., Coad, L., Milner-Gulland, E.J., 2009. Evidence for shifting baseline syndrome in conservation. Conserv. Lett. 2, 93–100. https://doi:10.1111/j.1755-263X.2009.00049.x.
Pauly, D., 1995. Anecdotes and the shifting baseline syndrome of fisheries. Trends Ecol. Evol. 10, 430. https://doi.org/10.1016/S0169-5347(00)89171-5.
Peixoto, F., 2005. Comparative effects of the Roundup and glyphosate on mitochondrial oxidative phosphorylation. Chemosphere 61, 1115–1122. https://doi.org/10.1016/j.chemosphere.2005.03.044.
Poole, J., Granli, P., 2022. The Gorongosa elephants through war and recovery: tusklessness, population size, structure and reproductive parameters. PACHYDERM 3, 38–54. ISSN:1026-2881.
Raman, P., 2014. Chlorothalonil. In: Wexler, P. (Ed.), Encyclopedia of Toxicology, third ed., pp. 919–922. https://doi.org/10.1016/B978-0-12-386454-3.00283-9 Science Direct.
Rich, A.L., Phipps, L.M., Tiwari, S., Rudraraju, H., Dokpesi, P.O., 2016. The increasing prevalence in intersex variation from toxicological dysregulation in fetal reproductive tissue differentiation and development by endocrine-disrupting chemicals. Environ. Health Insights 10, 163–171. https://doi:10.4137/EHI.S39825.
Rolland, R.M., 2000. A review of chemically-induced alterations in thyroid and vitamin A status from field studies of wildlife and fish. J. Wildl. Dis. 36, 15–35. https://doi.org/10.7589/0090-3558-36.4.615.
Rollor 3rd, E.A., 1993. Syndactylism and brachygnathia in a white-tailed deer. J. Wildl. Dis. 29, 618–619. https://doi:10.7589/0090-3558-29.4.618.
Romano, M.A., Romano, R.M., Santos, L.D., Wisniewski, P., Campos, D.A., de Souza, P.B., Viau, P., Bernardi, M.M., Nunes, M.T., de Oliveira, C.A., 2012. Glyphosate impairs male offspring reproductive development by disrupting gonadotropin expression. Arch. Toxicol. 86, 663–673. https://doi.org/10.1007/s00204-011-0788-9.
Romano, R.M., Romano, M.A., Bernardi, M.M., Furtado, P.V., Oliveira, C.A., 2010. Prepubertal exposure to commercial formulation of the herbicide Glyphosate alters testosterone levels and testicular morphology. Arch. Toxicol. 84, 309–317. https://doi.org/10.1007/s00204-009-0494-z.
Rondanelli, M., Faliva, M., Peroni, G., Infantino, V., Gasparri, C., Iannello, G., Perna, S., Riva, A., Petrangolini, G., Tartara, A., 2021. Essentiality of manganese for bone health: an overview and update. Nat. Prod. Commu. 16. https://doi:10.1177/1934578X211016649.
Saiz Pineda, J.F., 2018. Illustrated Guide to Prognathism in Cattle and Other Abnormalities of the Bite, first ed. Editorial Página Seis, Zapopan, Mexico, p. 212.
Samsel, A., Seneff, S., 2013. Glyphosate's suppression of cytochrome P450 enzymes and amino acid biosynthesis by the gut microbiome: pathways to modern diseases. Entropy 15, 1416–1463. https://doi.org/10.3390/e150416.
Samsel, A., Seneff, S., 2015. Glyphosate, pathways to modern diseases III: manganese, neurological diseases, and associated pathologies. Surg. Neurol. Int. 6, 45. https://doi:10.4103/2152-7806.153876.
Schreinemachers, D.M., 2003. Birth malformations and other adverse perinatal outcomes in four U.S. wheat-producing states. Environ. Health Perspect. 111, 1259–1264. https://doi:10.1289/ehp.5830.
Schutte, J.G., van den Ingh, T.S., 1997. Microphthalmia, brachygnathia superior, and palatocheiloschisis in a foal associated with griseofulvin administration to the mare during early pregnancy. Vet. Q. 19, 58–60. https://doi:10.1080/01652176.1997.9694741.

Self, S., Zhao, J., Holasek, R., Torres, R.C., King, A.J., 1996. The atmospheric impact of the Mount Pinatubo eruption. In: Newhall, C.G., Punongbayan, R.S. (Eds.), Fire and Mud: Eruptions and Lahars of Mount Pinatubo. University of Washington Press, Seattle, pp. 1089–1115.

Sharma, R.K., Goyal, A.K., 2014. Agro-pesticides and andrology. Int. J. Pharm. Pharmac. Sci. 6, 12–19. https://innovareacademics.in/journals/index.php/ijpps/article/view/2315.

Silver, M.K., Fernandez, J., Tang, J., McDade, A., Sabino, J., Rosario, Z., Vega, C.V., Alshawabkeh, A., Cordero, J.F., Meeker, J.D., 2021. Prenatal exposure to glyphosate and its environmental degradate, aminomethylphosphonic acid (AMPA), and preterm birth: a nested case–control study in the PROTECT cohort (Puerto Rico). Environ. Health Perspect. 129, 057011 https://doi.org/10.1289/EHP7295.

Singer, F.J., Singer, F.J., Harting, A., Symonds, K.K., Coughenour, M.B., 1997. Density dependence, compensation, and environmental effects on elk calf mortality in Yellowstone National Park. J. Wildlife Manage. 61, 12–25. https://doi:10.2307/3802410.

Smith, B.L., Williams, E.S., McFarland, K.C., McDonald, T.L., Wang, G., Moore, T.D., 2006. Neonatal Mortality of Elk in Wyoming: Environmental, Population, and Predator Effects. Department of Interior, U.S. Fish and Wildlife Service, Biological Technical Publication, Washington, D.C.:U.S, 2006. https://mcdonalddata.science/pubs/pub_smith2006.

Smith, D.W., Stahler, D.R., MacNulty, D.R., 2020. Yellowstone Wolves: Science and Discovery Book. University of Chicago Press, Chicago. ISBN-10 022672834x, ISBN-13 9780226728346.

Smith, D.W., Stahler, D.R., Cassidy, K.A., Stahler, E., Metz, M., Meyer, C., Rabe, J., Tatton, N., SunderRaj, J., Carroll, L., Jackson, M., Cassidy, B., Loggers, E., 2019. Yellowstone National Park Wolf Project Annual Report 2019. National Park Service, Yellowstone Center for Resources, Yellowstone National Park, WY, USA. YCR-2020-01. https://www.nps.gov/yell/learn/nature/upload/2019-WOLF-REPORT_508.pdf.

Sonne, C., Siebert, U., Gonnsen, K., Desforges, P., Eulaers, I., Persson, S., Roos, A., Bäcklin, M., Kauhala, K., Olsen, M.T., Harding, K.C., Treu, G., Galatius, A., Andersen-Ranberg, E., Gross, S., Lakemeyer, J., Lehnert, K., Lam, S.S., Peng, W., Dietz, R., 2020. Health effects from contaminant exposure in Baltic Sea birds and marine mammals: a review. Environ. Internatl. 139. UNSP 105725. https://doi:10.1016/j.envint.2020.105725.

Soto-Blanco, B., Gorniak, S.L., 2004. Prenatal toxicity of cyanide in goats: a model for teratological studies in ruminants. Theriogenology 62, 1012–1026. https://doi:10.1016/j.theriogenology.2003.12.023.

Spatola, G.J., Buckley, R.M., Dillon, M., Dutrow, E.V., Betz, J.A., Pilot, M., Parker, H.G., Bogdanowicz, W., Thomas, R., Chyzhevskyi, I., Milinevsky, G., Kleiman, N., Breen, M., Ostrander, E.A., Mousseau, T.A., 2023. The dogs of Chernobyl: Demographic insights into populations inhabiting the nuclear exclusion zone. Sci. Adv. 9, eade2537. https://doi:10.1126/sciadv.ade2537.

Staley, B.P., van der Lugt, J.J., Axsel, G., Loock, A.H., 1994. Congenital skeletal malformations in Holstein calves associated with putative manganese deficiency. J. S. Afr. Vet. Assoc. 65, 73–78. https://hdl.handle.net/10520/AJA00382809_1529.

Stone, K., Rassmusen, E., Maier, T., 2019. Eagle project data for accident-killed white-tailed deer 2018–2019. Unpublished PDF available online at. https://judyhoy.com/.

Swanson, N.L., Leu, A., Abrahamson, J., Wallet, B., 2014. Genetically engineered crops, glyphosate and the deterioration of health in the United States of America. J. Org. Syst. 9, 6–37. ISSN 1177-4258. https://www.organic-systems.org/journal/92/JOS_Volume-9_Number-2_Nov_2014-Swanson-et-al.pdf.

Szent-Györgyi, A., 1972. Dionysians and apollonians. Science 176 (4038), 966. https://doi:10.1126/science.176.4038.966.

Thelin, G.P., Stone, W.W., 2013. Estimation of Annual Agricultural Pesticide Use for Counties of the Conterminous United States, 1992–2009. U.S. Geological Survey Scientific Investigations Report, p. 54, 2013-5009.

Thompson, D.A., Lehmler, H.-J., Kolpin, D.W., Hladik, M.L., Vargo, J.D., Schilling, K.E., LeFevre, G.H., Peeples, T.L., Poch, M.C., LaDuca, L.E., Cwiertny, D.M., Field, R.W., 2020. A critical review on the potential impacts of neonicotinoid insecticide use: current knowledge of environmental fate, toxicity and implications for human health. Environ. Sci.: Process. Impacts 22, 1315–1346. https://doi.org/10.1039/C9EM00586B.

Thuermer, A., 2017. Hungry like the wolf? Here's just how hungry wolves are. Adventure Journal. March 29, 1, 2017. https://www.adventure-journal.com/2017/03/hungry-like-wolf-heres-just-hungry-wolves/.

Treves, A., Santiago-Avila, F.J., 2023. Estimating wolf abundance with unverified methods. Acad. Biol 1. https://doi.org/10.20935/AcadBiol6099.

Tuormaa, T.E., 1996. The adverse effects of manganese deficiency on reproduction and health: a literature review. J. Orthomolecular Med. 11, 84–86. https://api.semanticscholar.org/CorpusID:32749756.

Unsworth, J., Pac, D.F., White, G.C., Bartmann, R.M., 1999. Mule deer survival in Colorado, Idaho, and Montana. J. Wildlife Manage. 63, 315–326. https://doi.org/10.2307/3802515.

Usenko, S., Massey Simonich, S.L., Hageman, K.J., Schrlau, J.E., Geiser, L., Campbell, D. H., Appleby, P.G., Landers, D.H., 2010. Sources and deposition of polycyclic aromatic hydrocarbons to Western US National Parks. Environ. Sci. Technol. 44, 4512–4518. https://doi:10.1021/es903844n.

USGS National Water Quality Assessment. The pesticide national synthesis project. https://water.usgs.gov/nawqa/pnsp/usage/maps/compound_listing.php. (Accessed 18 February 2024).

U.S. National Pesticide Information Center. http://npic.orst.edu/factsheets/imidagen.html. (Accessed 18 February 2024).

Van Bruggen, A.H.C., He, M.M., Shin, K., Mai, V., Jeong, K.C., Finckh, M.R., Morris Jr., J. G., 2018. Environmental and health effects of the herbicide glyphosate. Sci. Total Environ. 616–617, 255–268. https://doi:10.1016/j.scitotenv.2017.10.309.

Vanlaeys, A., Dubuisson, F., Seralini, G.E., Travert, C., 2018. Formulants of glyphosate-based herbicides have more deleterious impact than glyphosate on TM4 Sertoli cells. Toxicol. Vitro 52, 14–22. https://doi:10.1016/j.tiv.2018.01.002.

Vucetich, J.A., Smith, D.W., Stahle, D.R., 2005. Influence of harvest, climate and wolf predation on Yellowstone elk, 1961–2004. Oikos 111, 259–270. https://doi.org/10.1111/j.0030-1299.2005.14180.x.

White, P.J., Garrott, R.A., 2005. Yellowstone's ungulates after wolves—expectations, realizations, and predictions. Biol. Conserv. 125, 141–152, 2005. https://mammals.indianbiodiversity.org/node/15149.

White, P.J., Bruggeman, J.E., Garrott, R.A., 2007. Irruptive population dynamics in Yellowstone pronghorn. Ecol. Applicat. 17, 1598–1606. https://doi.org/10.1890/06-2032.1.

Wilcox, C., 2014. Why are yellowstone's elk disappearing? Discover Magazine. https://www.discovermagazine.com/planet-earth/why-are-yellowstones-elk-disappearing. (Accessed 17 April 2014).

Zeid, E.H.A., Alam, R.T.M., Ali, S.A., Hendawi, M.Y., 2018. Dose-related impacts of imidacloprid oral intoxication on brain and liver of rock pigeon (*Columbia livia domestica*), residues analysis in different organs. Ecotox. Environ. Safe. 167, 60–68. https://doi:10.1016/j.ecoenv.2018.09.121.

Zhang, H., Bai, X., Zhang, T., Song, S., Zhu, H., Lu, S., Kannan, K., Sun, H., 2022. Neonicotinoid insecticides and their metabolites can pass through the human placenta unimpeded. Environ. Sci. Technol. 56 (23), 17143–17152. https://doi:10.1021/acs.est.2c06091.

Zhang, Q., Ji, C., Yan, L., Lu, M., Lu, C., Zhao, M., 2016. The identification of the metabolites of chlorothalonil in zebrafish (*Danio rerio*) and their embryo toxicity and endrocrine effects at environmentally relevant levels. Environ. Pollut. 218, 8–15. https://doi.org/10.1016/j.envpol.2016.08.026.

Zobiole, L.H.S., de Oliveira Jr., R.S., Huber, D.M., Constantin, J., de Castro, C., de Oliveira, F.A., de Oliveira Jr., A., 2010. Glyphosate reduces shoot concentrations of mineral nutrients in glyphosate-resistant soybeans. Plant Soil 28, 57–69. https://doi:10.1007/s11104-009-0081-3.