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Review:

Contamination Status and Toxicological Implications of Persistent Toxic Substances in Avian Species

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The present study reviewed the contamination status and accumulation features of persistent toxic substances (PTSs), such as polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), biphenyls (PCBs), and polybrominated diphenyl ethers (PBDEs), in avian species from Japan and open sea areas. PTSs were detected not only in Japanese coastal and inland birds but also in open sea birds, suggesting global-scale pollution by these contaminants. Higher concentrations of PBDEs were observed in Japanese raptor and omnivore species, while PCB levels in piscivorous birds were notably higher than in other species. Interestingly, relatively high concentrations of dioxins and related compounds (DRCs) such as PCDDs, PCDFs, and dioxin-like PCBs (DL-PCBs) were found in open sea birds, such as albatross species. Toxic equivalents (TEQs) of PCDDs, PCDFs, and DL-PCBs, which were calculated using toxic equivalency factors (TEFs) for birds proposed by the World Health Organization (WHO), were greater in albatross eggs than some avian toxicity thresholds, implying possible biochemical alterations by DRCs in albatross embryos. These results indicate that many avian species inhabiting Japan and the open ocean have been exposed to region-specific PTSs that may have put them at risk.

Keywords: persistent toxic substances, avian species, open ocean, Japan

1. Introduction

It is well known that persistent organic pollutants (POPs), such as polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), and biphenyls (PCBs) (**Fig. 1**), are endocrine disruptors. These contaminants have been found in wildlife and humans because of their persistency in the environment and highly bioaccumulative nature [1]. Especially, higher-trophic wildlife such as raptorial and piscivorous birds predominantly accumulate POPs and hence their toxic impacts are of great concern [1, 2]. In previous studies on wild avian species, significant POPs concentration-dependent relationships were observed for biochemical alteration and reduced reproductive success [3–6].

During the recent decade, our group has conducted comprehensive investigations on POPs in various birds inhabiting Asian regions and found higher concentrations of PCBs in Japanese birds, whereas organochlorine insecticides, such as dichlorodiphenyltrichloroethane and its metabolites (DDTs) and hexachlorocyclohexane isomers (HCHs), were predominant in avian species from some developing counties [7–11]. In addition, we demonstrated that Asian migratory birds reflected not only POPs pollution in sampled areas but also those in their stopover sites, breeding or wintering grounds, while resident birds directly reflected local pollution status of sampled areas [8, 9, 11, 12]. A few Asian migratory species collected from their breeding grounds accumulated considerable PCB levels, by which biochemical effects on their embryos may occur [13]. Furthermore, our group found that pelagic birds, such as albatross (*Diomedeidae*), inhibiting the North Pacific Ocean accumulated notably higher concentrations of POPs than specimens from Southern Ocean, and especially elevated PCB levels were observed [14], suggesting the transportability of these contaminants. However, studies on dioxins and related compounds (DRCs), such as PCDDs, PCDFs, and dioxin-like PCBs (DL-PCBs; which have a planar structure with no or a single chlorine atom on *ortho*-position), remain meager in Asian and pelagic birds compared to North America and Europe.

Recently, polybrominated diphenyl ethers (PBDEs) (**Fig. 1**) draw international attention as candidate substances of POPs. PBDEs, which are in use as brominated flame retardants (BFRs), are ubiquitous in the environment and have bioaccumulative nature [15], as is the case with POPs. Therefore, elevated PBDE levels have been detected in high trophic animals such as marine mammals and predacious birds [16]. Although detailed information on toxic effects are still lacking, it has been shown that PBDEs potentially cause adverse effects, such as clinical, morphological, immunological, and behavioral changes, disturbance of thyroid hormone homeostasis, and enzyme induction in *in vivo* and *in vitro* studies using experimental mammals and human cell lines [17–19]. In avian species such as glaucous gull (*Larus hyperboreus*) [20] and American kestrel (*Falco sparverius*) [21–23], disturbances of circulating reproductive hormone (proges-

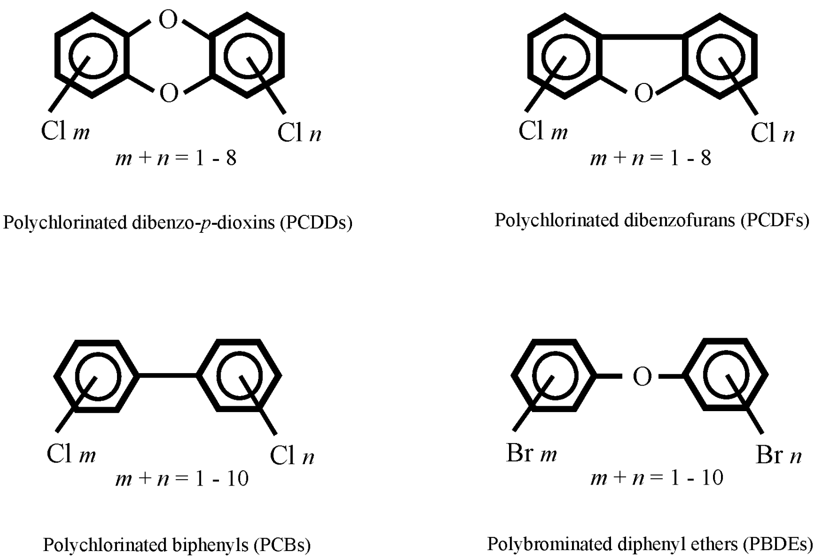

Fig. 1. Chemical structures of persistent toxic substances focused on this study.

terone) and thyroid hormone homeostasis, immunomodulation, oxidative stress, and developmental changes by PBDEs exposure have been observed. In North America and Europe, a large number of studies have been conducted on PBDEs contamination in some avian species, mainly in eggs [15, 16]. In addition, PBDEs have been detected in birds inhabiting the Arctic [20, 24], suggesting the transportability of these chemicals. However, very scarce investigations have been performed on PBDEs in avian species inhabiting Asian regions including Japan and open sea areas, although contamination status of PBDEs have been investigated in Japanese humans [25].

Based on this background, our group conducted studies on the contamination status and risk assessment of DRCs in some birds inhabiting Japan and open sea areas [26–30]. In addition, we recently elucidated the spatial trend of PBDE levels and patterns in avian species [31], which were collected from the open sea, and Japanese inland and coastal areas and have been stored in the Environmental Specimen Bank of Ehime University (*es*-Bank) at −25°C [32]. In this paper, we concisely review the contamination features of persistent toxic substances (PTSs), such as PCBs, DRCs, and PBDEs, in avian species obtained from the above studies.

2. PCBs Contamination

Mean lipid-normalized concentrations of PCBs in the pectoral muscle of avian species from the open sea, and Japanese inland and costal areas reported recently [31] were shown in **Fig. 2**. Among open sea birds, concentrations of PCBs in black-footed albatross (*Diomedea nigripes*) were highest, followed by Laysan albatross (*Diomedea immutabilis*) and northern fulmar (*Fulmarus glacialis*). Higher accumulation levels of PCBs in black-footed albatross than in other two species could be due to their different feeding habits. Black-footed albatross eats mainly fish and also human refuse, while Laysan albatross and northern fulmar eat mainly squid and amphipods, suggesting a higher position of black-footed albatross than other two species in the food web. In addition, as discussed in previous studies [26, 33], another possible reason might be the feeding of black-footed albatross in POPs contaminated areas containing higher PCB levels. Our previous studies also demonstrated that black-footed albatross accumulated higher levels of POPs than other open sea birds [14, 26, 30].

Among Japanese birds, higher PCB levels were observed in piscivorous species such as Steller's sea-eagle (*Haliaeetus pelagicus*) and common cormorant (*Phalacrocorax carbo*) than in goshawk (*Accipiter gentilis*), golden eagle (*Aquila chrysaetos*), jungle crow (*Corvus macrorhynchos*), and black-tailed gull (*Larus crassirostris*). We previously demonstrated remarkable accumulation of PCBs in fish-eating birds from Japan [11]. Thus, it is likely that PCBs pollution is greater in aquatic rather than in terrestrial environments and contamination by these compounds in fish may be considerable in Japan. Alternatively, Steller's sea-eagle might reflect PCBs exposure in Russia, a breeding ground for this species, in addition to Japan. Our previous study found that elevated PCB levels were detected in some environmental samples such as air, water, sediment, and soil from Russia, where higher amounts of PCBs were used in the past [34].

Interestingly, relatively high concentrations of PCBs were found in open sea birds, especially in black-footed albatross whose levels were higher than those in Japanese raptor species, although lower values than in Steller's sea-eagle and common cormorant were shown. This suggests that large amounts of PCBs have been already transported to remote open sea areas. Another study using skipjack tuna (*Katsuwonus pelamis*) as a bioindicator found relatively high PCB concentrations in specimens from some locations in the middle of the Pacific Ocean, indicating the expansion of PCB contamination on a global scale [35].

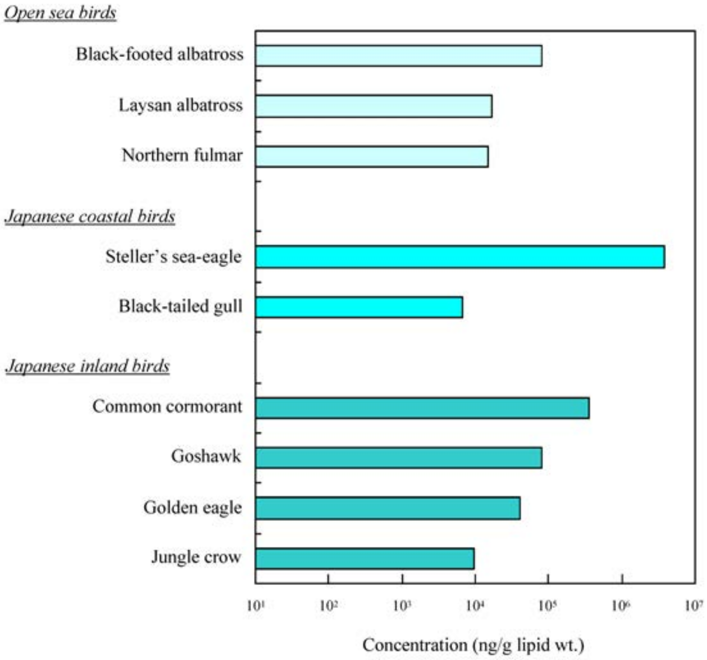

Fig. 2. Mean concentrations of PCBs in the pectoral muscle of birds from open sea, and Japanese coastal and inland areas.

Black-footed albatross, Japanese raptor and piscivorous species have accumulated elevated concentrations of PCBs, indicating that these avian species might be at high risk. However, limited information on risk assessments by PCBs for Japanese and open sea birds is available because of the constraints in sample collection, while studies on the induction of hepatic cytochrome P450 enzymes by DL-PCBs have been conducted in jungle crow [28] and common cormorant [36] from Japan. The development of studies on risk assessment by PCBs using avian biopsy samples need to be addressed.

3. Accumulation Features of Dioxins and Related Compounds

Our group has recently investigated contamination status and accumulation features of DRCs, such as PCDDs, PCDFs, and DL-PCBs (non- and mono-*ortho* PCBs), in some open sea and Japanese avian species [26–30]. Mean lipid-normalized concentrations of DRCs in the pectoral muscle of these birds were shown in **Fig. 3**. Relatively high concentrations of DRCs were observed in open sea birds, black-footed, Laysan, and short-tailed (*Diomedea albatrus*) albatrosses, compared with Japanese birds, such as common cormorant, jungle crow and black-eared kite (*Milvus migrans*), suggesting that large amounts of these contaminants have already spread to open sea areas. Especially, concentrations of PCDFs in open sea birds were significantly higher than those in common cormorant, in which the highest DRC levels among Japanese birds were observed. When concentration ratios of PCDFs to PCDDs in these avian species were calculated, notably higher PCDFs/PCDDs ratios were found in open sea birds than in Japanese birds (**Fig. 4**). These results indicate higher transportability of PCDFs than PCDDs by air and water and specific exposure of open sea birds such as albatross to PCDFs. Our study using skipjack tuna also found PCDFs, but not PCDDs, in some open sea specimens, indicating higher transportability of PCDFs than PCDDs [37].

Toxic equivalents (TEQs) of PCDDs, PCDFs, and DL-PCBs, which were calculated using toxic equivalency factors (TEFs) for birds proposed by WHO [38], and compositions in avian species were shown in **Fig. 5**. As expected from DRC levels, notably higher TEQs were observed in open sea birds than in Japanese birds. Especially, contribution of PCDFs and non-*ortho* PCBs to TEQs were predominant in open sea birds, indicating higher risk by these contaminants for albatrosses. On the other hand, composition of TEQs in Japanese birds varied among species. Higher contribution of PCDD/DFs in jungle crow and non-*ortho* PCBs in common cormorant were found, and composition in black-eared kite was intermediate between those of the other two species (**Fig. 5**). Thus, it is likely that main constituent of risk by DRCs are different among Japanese birds, and this could be due to differences in their habitat and food habits. As described earlier, while piscivorous species such as common cormorant have been exposed to relatively high levels of DL-PCBs because of the highly PCBs-contaminated aquatic environment, it is suspected that greater PCDD/DFs pollution sources are present in the Japanese terrestrial environment and hence terrestrial species have accumulated elevated levels of these contaminants.

Our group has also analyzed DRCs in the liver in addition to the pectoral muscle of some avian species, and found specific accumulation of PCDD/DF congeners in the liver [27–29]. When concentration ratios of DRC congeners in the liver to the pectoral muscle (L/M ratios)

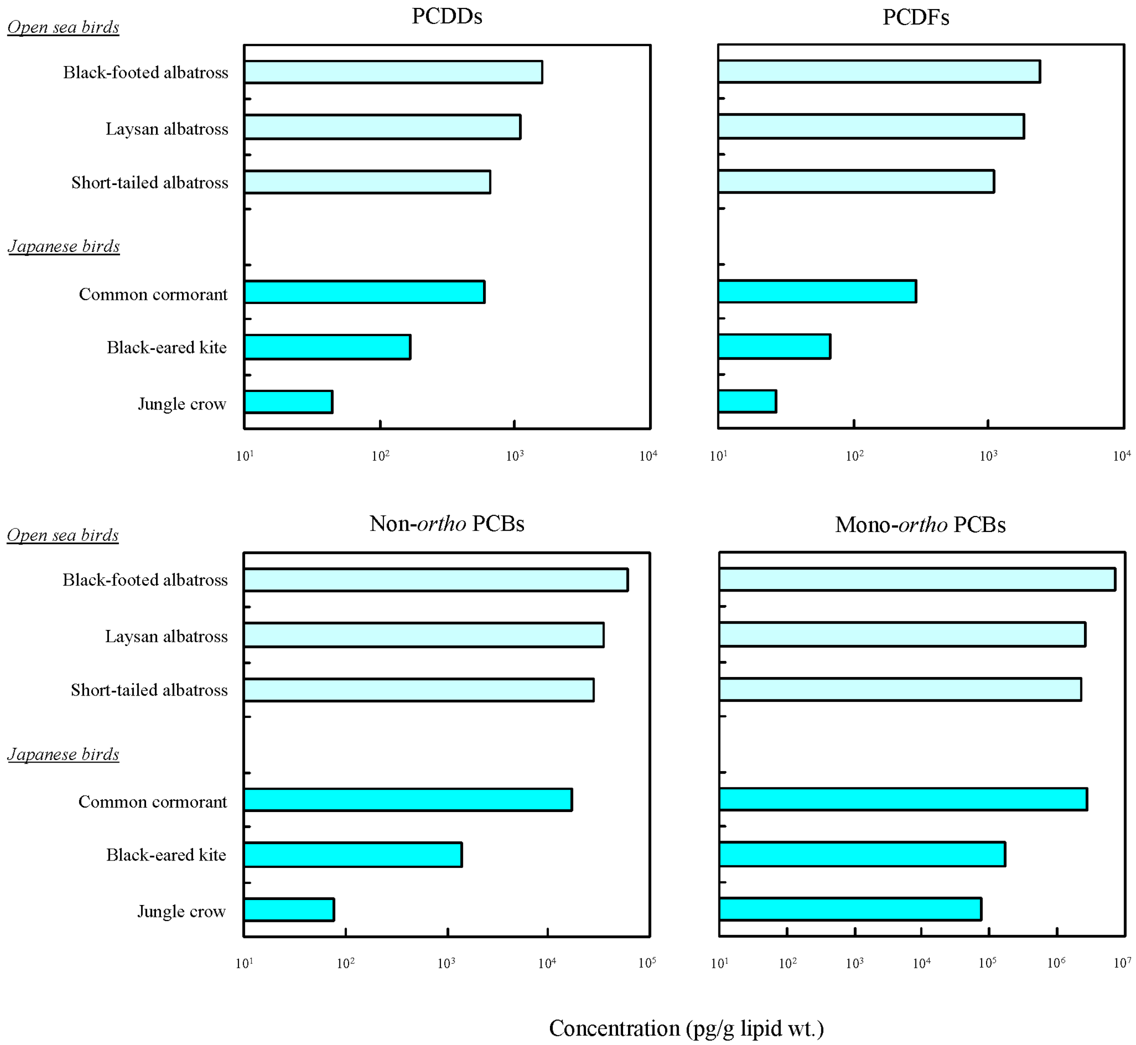

Fig. 3. Mean concentrations of PCDDs, PCDFs, and DL-PCBs (non- and mono-ortho PCBs) in the pectoral muscle of open sea and Japanese birds.

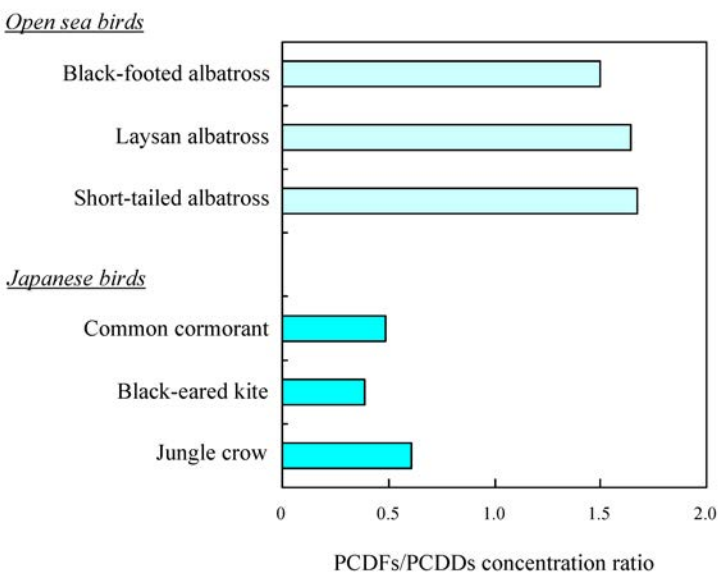

Fig. 4. Concentration ratios of PCDFs to PCDDs in open sea and Japanese birds.

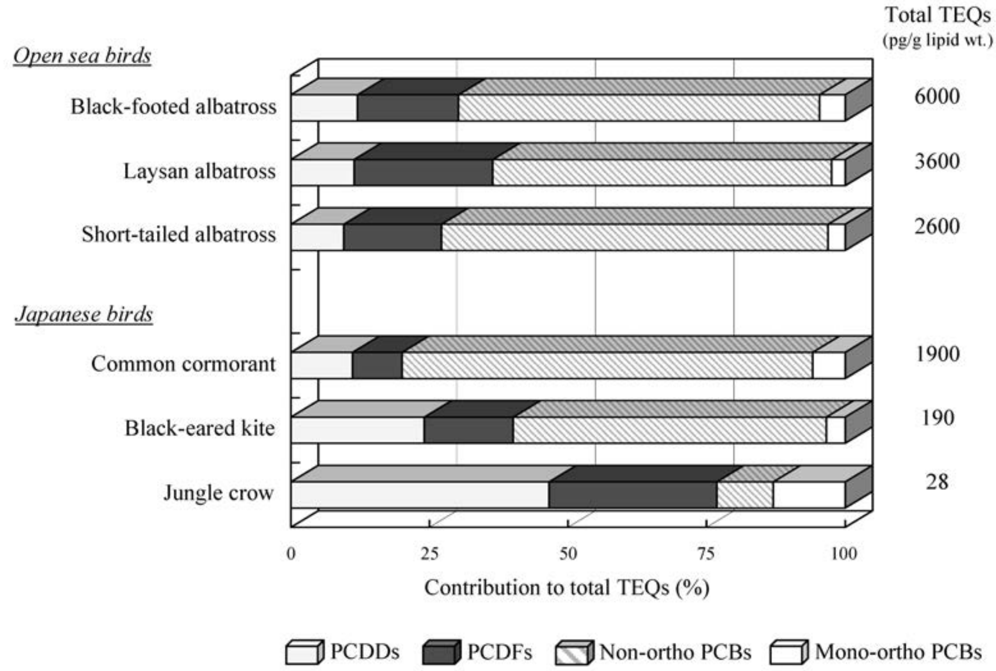

Fig. 5. Total toxic equivalent (TEQ) levels of PCDDs, PCDFs, and DL-PCBs and the compositions in open sea and Japanese birds.

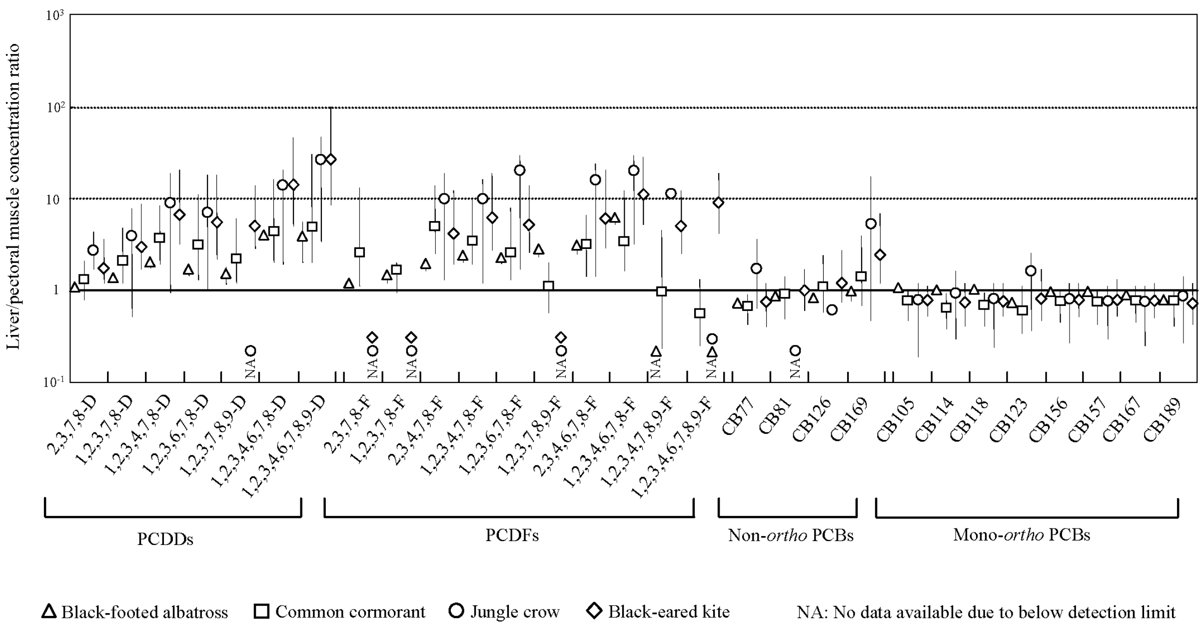

Fig. 6. Liver to pectoral concentration ratios of PCDD, PCDF, and DL-PCB congeners in open sea and Japanese birds.

were examined, L/M ratios of almost all the PCDD/DF congeners exceeded 1.0, whereas those of DL-PCB congeners except CB169 were around 1.0 (**Fig. 6**), suggesting hepatic sequestration of PCDD/DF congeners in avian species. Interestingly, L/M ratios of PCDD congeners tended to increase with the number of chlorine substitution. Such a hepatic sequestration of PCDD/DFs has also been found in wild mammalian species [39, 40]. Recent experimental studies using CYP1A2 knockout mice demonstrated that CYP1A2 was the target binding protein responsible for hepatic sequestration of some PCDD/DF congeners [41]. Therefore, our group examined relationships between L/M ratios of DRC congeners and hepatic CYP1A-like protein levels in jungle crow [28], black-eared kite [29], and common cormorant [36], and found that the L/M ratios of almost all the PCDD/DF congeners increased with CYP1A-like protein expression levels, indicating that the CYP1A-like protein, CYP1A5 as observed in jungle crow [28], might be involved in hepatic sequestration of PCDD/DFs in avian species. Thus, it can be speculated that avian liver is one of target organs for dioxin-induced toxicity, but the toxic potential by hepatic sequestration of PCDD/DFs remains unclear.

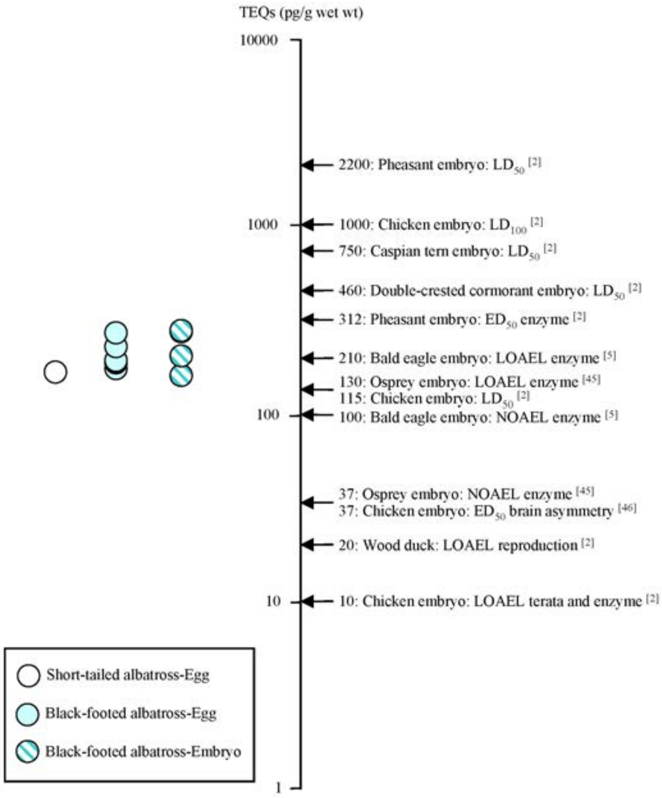

Fig. 7. TEQs in black-footed and short-tailed albatross eggs and toxicity thresholds for avian species. [2], [5], [45], and [46] represent references cited.

4. Toxic Equivalent Concentrations and Toxic Potential in Eggs

The avian embryo is generally considered more sensitive to dioxin toxicity than the adult bird. A recent study using chicken (*Gallus domesticus*) indicated that 2,3,7,8-tetrachlorinated dibenzo-*p*-dioxin (TCDD) treatment at earlier developmental stage of embryo was more sensitive for embryonic toxic effects, especially on hepatic and cardiac malfunction [42, 43]. Consequently, determination of TEQs in wild avian eggs may provide important information for their toxicological assessment. As described earlier, albatrosses have accumulated elevated concentrations of DRCs, and hence we evaluated toxic potential of DRCs by estimating TEQs in the eggs of black-footed and short-tailed albatross [30]. When TEQs on wet weight basis in these albatross eggs by using TEFs for birds [38] were estimated, mean TEQs in black-footed and short-tailed albatross eggs were 210 pg/g and 160 pg/g, respectively. These TEQ values were comparable to those in piscivorous bird eggs from the Great Lakes, which has been heavily contaminated by DRCs [44], implying that albatross embryos might be at high toxicological risk by these contaminants.

Until now, in some studies on wild avian species, significant DRC concentration-dependent relationships were observed for biochemical alteration in embryos and nestlings and reduced reproductive success [3–6]. Based on several studies using chicken and wild birds, toxicity thresholds of TEQs for some avian embryos have been estimated [2, 5, 45, 46]. When TEQs in black-footed and short-tailed albatross eggs were compared with these toxicity thresholds, the values in black-footed and short-tailed albatross eggs exceeded LD_{50} (115 pg/g) of chicken embryo and LOAEL (lowest-observed-adverse-effect-level) (130 pg/g) estimated from cytochrome P450 enzyme-induction in osprey embryo, and comparable to or higher than LOAEL (210 pg/g) estimated from cytochrome P450 enzyme-induction in bald eagle embryo (**Fig. 7**). A study using primary hepatocyte cultures of bald eagle embryos to determine their sensitivity to induction of cytochrome P4501A (CYP1A) by TCDD indicated that bald eagle hepatocytes from embryos were less sensitive to CYP1A induction than any other species such as gull, turkey, tern, pheasant, and chicken [47]. Hence, it is noteworthy that TEQs in black-footed and short-tailed albatross eggs exceeded LOAEL of bald eagle embryo. Considering these observations, it could be assumed that biochemical alterations by DRCs have potentially occurred in black-footed and short-tailed albatross embryos. However, it has been reported through *in ovo* [48] and *in vitro* experiments using primary hepatocyte cultures [49, 50] that sensitivity for biochemical effects such as CYP1A-induction by DRCs vary with avian species. Chicken is more sensitive than wild avian species, possibly followed by cormorant $>$ gull $>$ tern [48–50]. Furthermore, it was reported that RPFs (relative potency factors) estimated from CYP1A-induction (ethoxyresorufin-*O*-deethylase [EROD] activity) of 2,3,4,7,8-P_5CDF and CB77 to TCDD widely varied with avian species [50]. Because TEQs in black-footed and short-tailed albatross eggs were estimated using WHO-TEF, the certainty of risk for these albatross species could not be assessed. However, our group has recently cloned and sequenced two distinct AhR isoforms from the liver of black-footed albatross [51] and found significantly positive correlations between PCDD/DF congener-specific TEQs and EROD activity in the liver [52], indicating potential dioxin-like toxic alterations via AhR(s) in albatross species.

5. Spatial Trends of PBDEs Contamination

We have also conducted a survey on contamination status and accumulation features of PBDEs, which are considered candidate POPs, in avian species from the open sea, and Japanese inland and coastal areas [31]. PBDEs were detected in all the avian species analyzed, suggesting that PBDEs pollution has spread not only to Japanese inland and coastal areas but also to remote open sea areas, as in the case of PCBs and DRCs. Among open sea birds, mean concentrations (lipid weight basis) of PBDEs in black-footed albatross were highest, followed by Laysan albatross and northern fulmar (**Fig. 8**). Higher accumulation levels of PBDEs in black-footed albatross than in other two species could be due to their different feeding habits, *i.e.* the higher position of black-footed albatross in the food web, as described earlier.

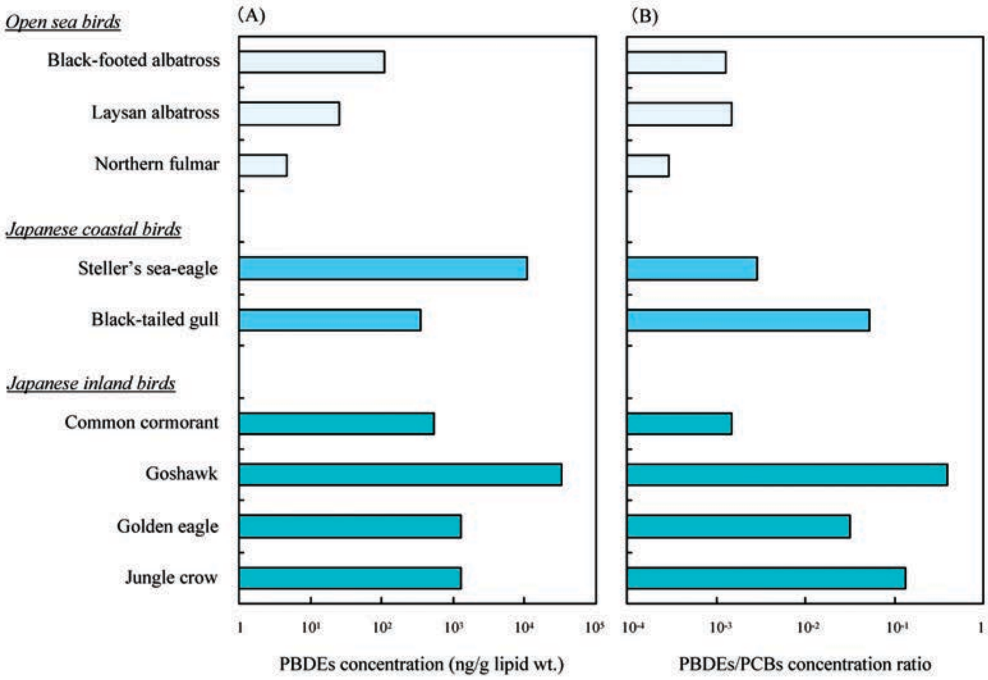

Fig. 8. Mean concentrations of PBDEs (A) and concentration ratios of PBDEs to PCBs (B) in the pectoral muscle of birds from open sea, and Japanese coastal and inland areas.

Among Japanese coastal and inland birds, goshawk accumulated the highest concentrations of PBDEs, followed by Steller's sea-eagle, jungle crow, golden eagle, common cormorant, and black-tailed gull (**Fig. 8**). Higher PBDE levels in raptors indicate the possible bioconcentration of these contaminants mainly through the food chain. Elevated PBDE levels in raptor species have also been reported in Belgium [53] and China [55]. Interestingly, concentrations of PBDEs in jungle crow were higher than those in common cormorant, a fish-eating bird, and comparable to those in golden eagle, implying that greater pollution sources of PBDEs may be present in the Japanese terrestrial environment close to human habitation.

Japanese coastal and inland birds accumulated higher PBDE levels than open sea birds did (**Fig. 8**), whereas concentrations of PCBs in open sea birds were relatively high compared to those in Japanese birds, as described earlier (**Fig. 2**). When concentration ratios of PBDEs to PCBs (PBDEs/PCBs ratios) in birds were calculated, coastal and inland species showed higher ratios than open sea birds (**Fig. 8**), indicating continuous input of PBDEs into the Japanese environment or lower transportability of PBDEs than PCBs. Such a trend was also reported by Elliot et al. [55]. They showed that PBDE concentrations in eggs of Leach's storm petrel (*Oceanodroma leucorhoa*), a marine species, were apparently lower than those in great blue heron, double-crested cormorant (*Phalacrocorax auritus*), and osprey (*Pandion haliaetus*) from British Columbia, while PCB levels were comparable, and concluded a relatively lower loading of PBDEs pollution in marine environment at present [55]. Our studies using skipjack tuna as a bioindicator demonstrated similar atmospheric transportability of PBDEs to PCBs [55, 56]. Considering higher PBDEs/PCBs ratios in the terrestrial species, goshawk and jungle crow, among all the birds analyzed (**Fig. 8**) and the above observations, it is likely that recent input of PBDEs into the Japanese terrestrial environment could be a main cause of higher ratios in coastal and inland birds than in open sea birds.

Despite being coastal and inland species, PBDEs/PCBs ratios in Steller's sea-eagle and common cormorant were relatively lower (**Fig. 8**). As described earlier, this could be due to markedly elevated PCB levels in these strong piscivorous birds (**Fig. 2**), because greater pollution sources of PCBs are still present in the Japanese aquatic environment and/or Russian regions. However, higher PBDEs/PCBs ratios were observed in black-tailed gull, a fish-eating bird (**Fig. 8**). This may be attributed to the fact that this species reflect PBDEs exposure on its migratory route, the coastal areas of East China and Korea. Our group recently demonstrated that relatively high concentrations of PBDEs were detected in the eggs of coastal birds from China [57]. To our knowledge, no study on PBDEs in Korean coastal birds is available, but our group found elevated PBDE levels in some blue mussels (*Mytilus edulis*) from Korean coastal waters [58].

Thus, Japanese avian species, especially high trophic raptor species, have accumulated higher concentrations of PBDEs, indicating that these birds might be at high risk. Less information on toxic potential by PBDEs for avian species, especially wild birds, is available so far, although disturbances of thyroid hormone homeostasis, immunomodulation, oxidative stress, and developmental changes by PBDEs exposure *in ovo* and during 29 days posthatch have been observed in American kestrel [21–23]. In these studies using American kestrel eggs, lipid-normalized concentrations of PBDEs in chick carcasses of the exposed group, which were analyzed at 36 days posthatch, were 796.18±119.52 ng lipid wt [21]. PBDE levels in Japanese raptor species and jungle crow analyzed by us were higher than those observed in the above American kestrel chicks, implying potential toxic effects by PBDEs for Japanese birds. However, this risk assessment includes the uncertainty of sensitivity to PBDEs toxicity by growth stage, because we analyzed PBDEs only in adult samples. Studies on risk assessment by PBDEs using Japanese avian eggs (embryos) and chicks (nestlings) are needed.

6. Conclusions

We elucidated the concentration status and accumulation features of PTSs in Japanese and open sea birds. Elevated concentrations of PCBs in Japanese piscivorous species were observed, indicating greater PCBs pollution in the Japanese aquatic environment. PTSs were detected not only in Japanese coastal and inland birds but also in open sea birds, indicating the global-scale pollution by these contaminants. Especially, concentrations of DRCs such as PCDFs and DL-PCBs in albatrosses were higher than those in Japanese birds. Besides, TEQs in albatross eggs exceeded some avian toxicity threshold values, implying that biochemical alterations by DRCs may occur in albatross embryos. On the other hand, Japanese birds, especially raptor species, accumulated notably higher levels of PBDEs than open sea birds, indicating that greater pollution sources of these contaminants are present in the Japanese environment. Our results suggest that detailed investigations on risk assessment by DRCs for open sea birds and by PBDEs for Japanese avian species are indispensable. Additionally, it is speculated that PBDEs released into the Japanese environment could be gradually transported to remote open sea areas as in the case of POPs, such as PCBs and DRCs, and hence investigations on temporal trend and risk assessment of PBDEs are required on pelagic animal species.

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