（様式５）

乳幼児健康調査（問診票）

（都府県名　　）

母 親 氏 名：
乳幼児氏名：

年　　齢：　　歳　　月（満１歳２ヶ月未満）

採血問診日：　　月　　日（医療機関及び医師名　　）

①採血時よりさかのぼって２週間以内に37．５℃以上の発熱がある。　ある　ない

②採血時よりさかのぼって２週間以内に風邪をひいた。　ある　ない

③採血時よりさかのぼって１ヶ月以内に予防接種を受けた。　ある　ない

母子健康手帳を確認し
誕生以来の全ての
予防接種を記入

予防接種の種類	接種月日

④過去に重い病気にかかったことがある。　ある　ない
（「ある」の場合の病名：　　）

⑤アレルギー疾患がある。　ある　ない
（「ある」の場合の病名：　　）

⑥採血時の体温　（　　℃）

⑦発育・発達状況
身体発育（生後　　月　　日）
体重　　g　身長　　ｃｍ　頭囲　　ｃｍ　胸囲　　ｃｍ
「乳幼児健康調査票（1歳児用）のⅡ発育発達」について確認をし、必要に応じ身体等のチェックを行う。
所見（　　）

⑧これまでの栄養状況
「乳幼児健康調査票（1歳児用）のⅢこれまでの栄養状況」について確認をし、必要に応じ調査票を訂正する。

⑨その他特記事項（　　）

注：①又は②で「ある」の場合、③において「ある」かつ１ヶ月以内にポリオや麻疹などの生ワクチンか２週間以内に生ワクチン以外の予防接種を受けた場合、⑤において37．５℃以上の体温がある場合は、いずれも当日の採血は中止し、予防接種又は37．５℃以上の発熱若しくは風邪が治ってから２週間以上期間を置いて改めて採血を行うこと。

＊　ただし、予防接種や発熱により、前述のとおりの調査日の設定がどうしても困難な場合には、検査結果は参考値になるが調査等を行うことを保護者に伝え、調査日を設定する。

第2(3)子の母乳採取時の第1(2)子の栄養および健康調査票

都府県名(　　)

母親氏名:　　連絡先:TEL
第1(2)子氏名:　　性別:男・女　　出生体重:　　g
生年月日:　　年　　月　　日(在胎　　週　　日または出産予定日　　月　　日)
第2(3)子氏名:　　性別:男・女　　出生体重:　　g
生年月日:　　年　　月　　日(在胎　　週　　日または出産予定日　　月　　日)

第1(2)子(まえのお子さん)についてお尋ねします:

Ⅰ　これまでに重い病気にかかったことがありますか　　:　ある　　ない
あった場合の病名:

Ⅱ　アレルギー疾患があるといわれたことがありますか　　:　ある　　ない
あった場合の病名:

Ⅲ　現在までの発育・発達

1)　身体発育(1歳近くでの測定日の月齢と測定値を記入して下さい):測定日(生後　月　日)
体重　　g　身長　　cm　頭囲　　cm　胸囲　　cm

2)運動発達:
次のことが出来るようになったのはいつですか。

(1)首のすわり	:生後　月	(4)つかまり立ち	:生後　月
(2)寝返り	:生後　月	(5)伝い歩き	:生後　月
(3)お座り	:生後　月	(6)一人歩き(2～3歩)	:生後　月

3)1歳の誕生日までに次の項目が出来ていたら○、出来なければ×、記憶に無ければ△を○で囲んで下さい。

(1)「いけません」というと、ちょっと手をひっこめる。　(○　×　△)
(2)「バイバイ」や「さよなら」に反応する。　(○　×　△)
(3)「おいで」「ちょうだい」「ねんね」などを1つでも理解できる。　(○　×　△)
(4)食物のことを「マンマ」という(他の有意義語でも良い)。　(○　×　△)
(5)ブラシ、鉛筆などを使うまねをする。　(○　×　△)

Ⅲ　1歳までの栄養状態を教えて下さい。
ほ乳方法はどうでしたか。次の番号をカッコ内に入れて下さい。
1. 母乳のみ　2. 混合(母乳が主)　3. 混合(母乳とミルクがほぼ等量)
4. 混合(人工が主)　5. 人工栄養のみ

生後1ヶ月未満	(ほ乳方法　　)	6～7ヶ月未満	(ほ乳方法　　)
1～2ヶ月　〃	(ほ乳方法　　)	7～8ヶ月　〃	(ほ乳方法　　)
2～3ヶ月　〃	(ほ乳方法　　)	8～9ヶ月　〃	(ほ乳方法　　)
3～4ヶ月　〃	(ほ乳方法　　)	9～10ヶ月　〃	(ほ乳方法　　)
4～5ヶ月　〃	(ほ乳方法　　)	10～11ヶ月　〃	(ほ乳方法　　)
5～6ヶ月　〃	(ほ乳方法　　)	11～12ヶ月　〃	(ほ乳方法　　)

(第2子以降の母乳採取に協力が得られた場合で前児が当研究班の1歳時乳幼児健康診査を受診しなかった場合に記入して下さい)

平成１８年度母乳中のダイオキシン類調査　問診票（様式１）

母親氏名：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

乳児氏名：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

住所：〒＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電話番号：＿＿＿＿＿－＿＿＿＿＿－＿＿＿＿＿

記入年月日：平成＿＿＿＿年＿＿＿＿月＿＿＿＿日

1. 母親の現状

生年月日：昭和＿＿＿＿年＿＿＿＿月＿＿＿＿日

身長：＿＿＿＿＿＿ ｃｍ　（本人の申告　大体の数値でよい）

妊娠直前の体重：＿＿＿＿＿＿ｋｇ　（本人の申告　大体の数値でよい）

出産日：平成＿＿＿＿＿年＿＿＿＿＿月＿＿＿＿＿日

出産場所（医療機関の場合には医療機関名，所在地，電話番号）

１．自宅
２．助産所
３．病院・診療所

名　称：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

所在地：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

電　話：＿＿＿＿＿＿＿－＿＿＿＿＿＿＿－＿＿＿＿＿＿＿

妊娠中のつわりの状況　１．ほとんどない　　２．軽度　　３．中等度　　３．重度
（本人の主観的判断でよい）

2. 母親本人の乳児期の状況

出生順位：＿＿＿＿＿＿ 人中の＿＿＿＿＿＿ 番目　（死産は含まない）

乳児期（生後３か月まで）の栄養　１．母乳のみ　２．混合栄養　３．ミルクのみ　４．不明

（ご本人から自分のお母様［産まれてくる子供からみたら母方祖母］にお尋ね下さい）
（ここの情報がどうしても得られない場合には，不明として下さい［記入漏れと区別のため］）

3. 居住歴（住民登録の場所ではなく，実際に住んでいた場所を尋ねる）

Ⅰ　現在の居住地

昭・平＿＿＿＿年＿＿＿月から現在に至る（上記の住所）
飲用や食事に使用する水は　１．水道水　　２．井戸水　　３．両方

II　過去の居住地（生まれたときまでさかのぼる）

昭・平＿＿＿年＿＿＿月から　昭・平＿＿＿年＿＿＿月まで
＿＿＿都・道・府・県＿＿＿市・郡＿＿＿区・町・村
＿＿＿丁目・番＿＿＿号＿＿＿
飲用や食事に使用する水は　1．水道水　2．井戸水　3．両方

昭・平＿＿＿年＿＿＿月から　昭・平＿＿＿年＿＿＿月まで
＿＿＿都・道・府・県＿＿＿市・郡＿＿＿区・町・村
＿＿＿丁目・番＿＿＿号＿＿＿
飲用や食事に使用する水は　1．水道水　2．井戸水　3．両方

昭・平＿＿＿年＿＿＿月から　昭・平＿＿＿年＿＿＿月まで
＿＿＿都・道・府・県＿＿＿市・郡＿＿＿区・町・村
＿＿＿丁目・番＿＿＿号＿＿＿
飲用や食事に使用する水は　1．水道水　2．井戸水　3．両方

出生時から　昭・平＿＿＿年＿＿＿月まで
＿＿＿都・道・府・県＿＿＿市・郡＿＿＿区・町・村
＿＿＿丁目・番＿＿＿号＿＿＿
飲用や食事に使用する水は　1．水道水　2．井戸水　3．両方

（欄が足りない場合には別紙に同じ様式で記入して下さい）

4．職業歴（ダイオキシンへの曝露を評価するので具体的な仕事の内容を記入して下さい）

I
昭・平＿＿＿年＿＿＿月から　昭・平＿＿＿年＿＿＿月まで
勤務先＿＿＿
具体的な仕事内容＿＿＿
（例えば，事務，運転手，ゴミ処理場での現場作業，など．以下も同様）

II
昭・平＿＿＿年＿＿＿月から　昭・平＿＿＿年＿＿＿月まで
勤務先＿＿＿
具体的な仕事内容＿＿＿

III
昭・平＿＿＿年＿＿＿月から　昭・平＿＿＿年＿＿＿月まで
勤務先＿＿＿
具体的な仕事内容＿＿＿

（欄が足りない場合には別紙に同じ様式で記入して下さい）

5. 喫煙歴

a．本人の喫煙歴　（建前ではなく実態を記入して下さい）

1．習慣的な喫煙はしたことがない（生涯において数本～数十本程度の喫煙歴を含む）
2．現在喫煙中
3．今回の妊娠のためにやめた（中断中も含む）
4．今回の妊娠以前にやめた
　その理由　a．病気
　　b．医療専門職のすすめ
　　c．その他（＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿）

2．3．4．の場合

喫煙した期間と1日の本数，主な銘柄

期間	本数	銘柄
＿＿歳から＿＿歳	1日約＿＿本	銘柄＿＿＿＿＿＿＿＿
＿＿歳から＿＿歳	1日約＿＿本	銘柄＿＿＿＿＿＿＿＿
＿＿歳から＿＿歳	1日約＿＿本	銘柄＿＿＿＿＿＿＿＿
＿＿歳から＿＿歳	1日約＿＿本	銘柄＿＿＿＿＿＿＿＿

（1日の本数，銘柄が変わった時には行を変えて記載して下さい）

b．受動喫煙

Ⅰ．小学生の時に，同居人の中で喫煙する人が　1．いなかった　2．いた（＿＿＿人）

Ⅱ．中学生の時に，同居人の中で喫煙する人が　1．いなかった　2．いた（＿＿＿人）

Ⅲ．現在の同居人の数は＿＿＿＿＿＿ 人（本人は含まない，a）

このうち，現在非喫煙者（やめた者も含む）　＿＿＿＿人　（b）
喫煙者だが家の中ではすわない者　＿＿＿＿人　（c）
喫煙者で家の中でも吸う者　＿＿＿＿人　（d）

（a＝b＋c＋dとなる）

6. 妊娠直前の健康状態，既往歴

子宮筋腫の既往歴　1．なし　2．あり（＿＿＿＿歳の時）
子宮内膜症の既往歴　1．なし　2．あり（＿＿＿＿歳の時）
アトピー性皮膚炎の既往歴　1．なし　2．あり（＿＿＿＿歳の時）
甲状腺疾患の既往歴　1．なし　2．あり（　　歳の時，病名：＿＿＿＿＿＿）

その他の既往歴（入院するような大きな疾患）

病名＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿　＿＿＿＿歳の時

病名＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿　＿＿＿＿歳の時

妊娠直前の健康状態

1．持病があった

病名＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿
　a．医師の管理下　　b．その他

2．健康であった

7. 食習慣

普段の生活（妊娠前）での食事習慣について、番号に○をつけて下さい.

1．肉	1．食べない	2．月に1～3回	3．週に1～2回
	4．週に3～4回	5．週に5～6回	6．毎日食べる
2．魚	1．食べない	2．月に1～3回	3．週に1～2回
	4．週に3～4回	5．週に5～6回	6．毎日食べる
3．牛乳	1．食べない	2．月に1～3回	3．週に1～2回
	4．週に3～4回	5．週に5～6回	6．毎日食べる
4．バター・チーズ	1．食べない	2．月に1～3回	3．週に1～2回
	4．週に3～4回	5．週に5～6回	6．毎日食べる
5．卵	1．食べない	2．月に1～3回	3．週に1～2回
	4．週に3～4回	5．週に5～6回	6．毎日食べる

8．母乳採取時の乳児の状況

母乳採取日：平成＿＿＿＿年＿＿＿＿月＿＿＿＿日

身体計測値（一ヶ月健診時あるいは直近のものを記入してください
計測月日＿＿＿＿月＿＿＿＿日）

体重：＿＿＿＿＿＿ g　身長：＿＿＿＿＿＿ cm

胸囲：＿＿＿＿＿＿ cm 頭囲：＿＿＿＿＿＿ cm

栄養方法：　母　乳　1．与えている　→　1日＿＿＿＿回

2．与えていない

人工乳　1．与えている　→　1回＿＿＿＿ml×1日＿＿＿＿＿＿回

2．与えていない

乳児健診受診　1．なし　2．あり

a．異常なし

b．異常あり（指摘された事項：＿＿＿＿）

児が罹患した病気　1．なし　2．あり（病名＿＿＿＿＿＿＿＿＿＿＿＿）

（ご協力ありがとうございました。同封の封筒でご返送下さい）

平成18年度厚生労働科学（食品の安心・安全確保推進）研究事業
「ダイオキシンの乳幼児への影響その他の汚染実態の解明に関する研究－特に母乳中のダイオキシン類濃度の経年的変化と乳幼児発育発達に及ぼす影響－」班

平成１８年度母乳中のダイオキシン類調査　医療機関記入調査票　（様式２）

母親氏名：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

(ﾌﾘｶﾞﾅ)
乳児氏名：＿＿＿＿＿＿＿＿＿＿＿＿＿＿　男・女

乳児の生年月日　平成＿＿＿＿年＿＿＿＿月＿＿＿＿日

調査年月日　平成＿＿＿＿年＿＿＿＿月＿＿＿＿日

１．妊娠・分娩の経過

在胎期間　：＿＿＿＿週＿＿＿＿日

分娩胎位　：　１．頭位　２．骨盤位　３．その他（＿＿＿＿＿＿＿＿）

帝王切開　：　１．なし　２．あり

妊娠合併症：　１．なし　２．あり（＿＿＿＿＿＿＿＿＿＿＿＿）

２．出生時の児の状態

出生時の計測値：　体重＿＿＿＿＿＿ｇ　身長＿＿＿＿＿＿ｃｍ

胸囲＿＿＿＿＿＿ｃｍ　頭囲＿＿＿＿＿＿ｃｍ

新生児仮死　：　１．なし
２．あり　→　アプガー・スコア＿＿＿＿点（１分）

＿＿＿＿点（５分）

３．早期新生児期の状態

早期新生児期の異常：　１．なし
２．あり（病名：＿＿＿＿＿＿＿＿＿＿＿＿）

先天性代謝異常検査：　１．未実施
２．実施済　→　結果：　１．異常なし
２．要再検査
（項目：＿＿＿＿＿＿）

（様式４）

乳幼児健康調査票（１歳児用）

（都府県名　　）

母親氏名：
乳幼児氏名：　　性別：男・女　出生体重：　　g　出生順位：第　　子
生年月日：　年　月　日（在胎　週　日または出産予定日　月　日）
出生場所（病院等の名称）：

Ⅰ　これまでにかかった病気：

Ⅱ　現在までの発育・発達
１）発育発達：
次のことが出来るようになったのはいつですか。

（１）首のすわり	：生後　月	（４）つかまり立ち	：生後　月
（２）寝返り	：生後　月	（５）伝い歩き	：生後　月
（３）お座り	：生後　月	（６）一人歩き（２～３歩）	：生後　月

２）１歳の誕生日までに次の項目が出来れば○、出来なければ×、試みたことがなければ△をつけて下さい。

（１）「いけません」というと、ちょっと手をひっこめる。　（○　×　△）
（２）「バイバイ」や「さよなら」に反応する。　（○　×　△）
（３）「おいで」「ちょうだい」「ねんね」などを１つでも理解できる。　（○　×　△）
（４）食物のことを「マンマ」という（他の有意義語でも良い）。　（○　×　△）
（５）ブラシ、鉛筆などを使うまねをする。　（○　×　△）

Ⅲ　これまでの栄養状態を教えて下さい。
１）ほ乳方法はどうでしたか。次の番号をカッコ内に入れて下さい。
１．母乳のみ　２．混合（母乳が主）　３．混合（母乳とミルクがほぼ等量）
４．混合（人工が主）　５．人工栄養のみ

生後１ヶ月未満	（ほ乳方法　）	６～７ヶ月未満	（ほ乳方法　）
１～２ヶ月　〃	（ほ乳方法　）	７～８ヶ月　〃	（ほ乳方法　）
２～３ヶ月　〃	（ほ乳方法　）	８～９ヶ月　〃	（ほ乳方法　）
３～４ヶ月　〃	（ほ乳方法　）	９～10ヶ月　〃	（ほ乳方法　）
４～５ヶ月　〃	（ほ乳方法　）	10～11ヶ月　〃	（ほ乳方法　）
５～６ヶ月　〃	（ほ乳方法　）	11～12ヶ月　〃	（ほ乳方法　）

Ⅳ　予防接種の接種状況を母子健康手帳から書き写して下さい。

予防接種の種類	接種月日

注意事項：調査予定日から２週間前以内に37.5℃以上の発熱や風邪をひいた場合又は予防接種を受けた場合には、必ず、下記までご連絡下さい。発熱や風邪が治りかつ予防接種日から２週間以上経過した日に調査日の変更を行います。
：母子健康手帳を忘れずにご持参下さい。

連絡先　　TEL

（様式５）

乳幼児健康調査（問診票）

（都府県名　　）

母親氏名：
乳幼児氏名：

年　　齢：　　歳　　月（満１歳２ヶ月未満）

採血問診日：　　月　　日（医療機関及び医師名　　）

①採血時よりさかのぼって２週間以内に37．５℃以上の発熱がある。　ある　ない

②採血時よりさかのぼって２週間以内に風邪をひいた。　ある　ない

③採血時よりさかのぼって１ヶ月以内に予防接種を受けた。　ある　ない

母子健康手帳を確認し誕生以来の全ての予防接種を記入

予防接種の種類	接種月日

④過去に重い病気にかかったことがある。　ある　ない
（「ある」の場合の病名：　　）

⑤アレルギー疾患がある。　ある　ない
（「ある」の場合の病名：　　）

⑥採血時の体温　（　　℃）

⑦発育・発達状況
身体発育（生後　　月　　日）
体重　　g　　身長　　ｃｍ　　頭囲　　ｃｍ　　胸囲　　ｃｍ
「乳幼児健康調査票（1歳児用）のⅡ発育発達」について確認をし、必要に応じ身体等のチェックを行う。
所見（　　）

⑧これまでの栄養状況
「乳幼児健康調査票（1歳児用）のⅢこれまでの栄養状況」について確認をし、必要に応じ調査票を訂正する。

⑨その他特記事項（　　）

注：①又は②で「ある」の場合、③において「ある」かつ１ヶ月以内にポリオや麻疹などの生ワクチンか２週間以内に生ワクチン以外の予防接種を受けた場合、⑤において37．５℃以上の体温がある場合は、いずれも当日の採血は中止し、予防接種又は37．５℃以上の発熱若しくは風邪が治ってから２週間以上期間を置いて改めて採血を行うこと。
＊　ただし、予防接種や発熱により、前述のとおりの調査日の設定がどうしても困難な場合には、検査結果は参考値になるが調査等を行うことを保護者に伝え、調査日を設定する。

Ⅳ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Uehara R, Guan P, Nakamura Y, Matsuura N, Kondo N, Tada H	Dioxins in human milk and smoking of mothers.	Chemosphere		in press	2007
多田裕	母乳と環境汚染:母乳を科学する	産婦人科の実際	56(3)	339-342	2007
Uehara R, Peng G, Nakamura Y,et al	Human milk survey for dioxins in the general population in Japan.	Chemoshere	62	1135-1141	2006
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H Kaneko、E Matsui、S Shioda、N Kawamoto、Y Nakamura、R Ueharai、N Matsuura、M Morita、H Tada, and N Kondo	Effects of dioxins on the quantitative levels of immune components in infants	Toxicology and Industrial Health	22	131-136	2006
伊藤尚志、横田行史、柴山啓子、大津成之、下浜真理子、狐崎雅子、剣持　学、野渡正彦、松浦信夫、川上祐次、石井正浩	濾紙血TSH、freeT4同時測定によるクレチン症スクリーニング-当院における5年間の結果-	日本マススクリーニング学会誌	16(3)	45-51	2006
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松浦信夫	新生児バセドウ病の発症-その危険性と防御策、治療法-	日本臨床	64(12)	2303-2307	2006
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Shibayama K, Ohyama Y, Yokota Y, Ohtsu S, Takubu N,Matsuura N.	Assays for thyroid-stimulating antibodies and thyrotropin- bidining Inhibitory immuno- globulins in children with Graves' disease.	Endocrine J	52	505-510	2005
Shibayama K, Ohyama Y, Hishinuma A, Yokota Y, Kazahari K, Kazahari M, Irie T, Matsuura N	Subclinical hypothyroidism caused by a mutation of the thyrotropin receptor gene.	Pediatr Intern	47	105-108	2005
松井永子、近藤直実、金子英雄、篠田紳司、川本典生、中村好一、松浦信夫、多田裕	母乳栄養とダイオキシン－母乳中のダイオキシンが母乳栄養児の免疫アレルギー反応に与える影響の有無について－	小児科診療,	153(3)	533-536	2005
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Ⅴ. 研究成果の刊行物・別刷

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Dioxins in human milk and smoking of mothers

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Abstract

Background: The relation between the levels of dioxins in human breast milk and the smoking habits of the mothers is controversial. To clarify this relationship, we analyzed data from the human milk survey in Japan.

Methods: The human milk survey has been conducted in Japan since 1997. Healthy pregnant women aged 20–39 years were recruited and 50 ml of breast milk was collected from them at 30 days after delivery. PCDDs, PCDFs, and dioxin-like PCBs were measured by using GC/MS. The smoking habits of the mothers were established by interviewing them soon after delivery and were classified into four categories: current smokers, ever smokers who quit smoking at the pregnancy, ever smokers who quit smoking before the pregnancy, and never smokers. The levels of dioxins in breast milk were compared in the four categories of smoking among 853 primiparas. In addition, we analyzed the association between dioxin levels and passive smoking among never smokers. The geometric means of the dioxin concentrations were calculated in order to compare the differences between dioxins.

Results: The geometric means of dioxin-like PCBs in milk of never smokers was the highest (9.2 pg TEQ/g fat); followed by ever smokers who quit smoking before the pregnancy, ever smokers who quit smoking at the pregnancy, and current smokers (7.5, 7.2, and 6.6 pg TEQ/g fat, respectively). The differences between these levels were statistically significant (ANOVA, $p < 0.001$). No significant difference was observed between the level of dioxins in milk from never smokers subjected to passive smoking status and those who had not experienced passive smoking.

Conclusion: The levels of dioxin-like PCBs in human milk were negatively related to the smoking habits of mothers.

Keywords: Cigarette smoking; Dioxins; Dioxin-like PCBs; Epidemiology; Human milk; Passive smoking

1. Introduction

The dioxin burden in the human body especially that of infants and children, has caused particular concern in recent years. A human milk survey has been conducted to monitor the levels of dioxins in the general population in Japan (Uehara et al., 2006). When the level of dioxins in human milk is being investigated, the smoking habits of the mothers should be considered to be a confounding factor, because dioxins, especially PCDDs, are contained in cigarette smoke (Muto and Takizawa, 1989). In addition, smoking during pregnancy is an important risk factor for maternal and fetal outcomes (Cnattingius, 2004). It is important to elucidate the association between cigarette smoking among mothers and dioxin levels in their milk. While dioxin levels in human milk among active smokers were lower than those among non-smokers (Fürst et al., 1992; Bates et al., 1994; Takekuma et al., 2004; Hedley et al., 2006), other studies showed no relation between smoking habits and dioxin levels (Rogan et al., 1986; Pluim

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et al., 1993). To elucidate the relationship between cigarette smoking among mothers and dioxin levels in their breast milk, we analyzed the data from The Human Milk Survey carried out in Japan.

2. Methods

2.1. Human milk survey in Japan

The human milk survey has been conducted in several prefectures and cities in Japan since 1997. The details of the survey carried out in various areas have been described in a previous report (Uehara et al., 2006). Healthy pregnant women aged between 20 and 39 years were recruited by public health nurses. A signed informed consent form was submitted to the public health nurses by all participants; 50 ml of breast milk was then collected manually from each participant at 30 days after delivery. PCDDs (seven isomers), PCDFs (10 isomers), and dioxin-like PCBs (12 isomers) were measured using gas chromatography and mass spectrometry at the Japan Food Research Laboratory. In brief, the milk samples were mixed with an aqueous solution of sodium oxalate, diethyl ether and ethanol and the mixture was extracted with hexane. The fat content was determined gravimetrically. Thereafter, a three-step clean-up procedure was performed by passing the sample through a column filled with silica gel, then through another column containing aluminum oxide, and finally through an activated charcoal column. After concentrating the sample, gas chromatography and mass spectrometry were employed to measure the contents. A mixture of ^{13}C-labelled PCDDs, PCDFs, and dioxin-like PCBs was used as an internal standard. The levels of dioxins were described on a fat basis and the toxic equivalence (TEQs) values were calculated by using toxic equivalent factors (TEFs) of 2,3,7,8-tetrachlorodibenzodioxin, which has previously been documented by WHO (Van den Berg et al., 1998). We analyzed the data of primiparas from 1998 to 2004 because only three isomers of dioxin-like PCBs had been measured in 1997. In this study, we only investigated data obtained from primiparas because the parity of nursing mothers was considered to be a confounder and the number of secundiparas was small.

2.2. Smoking habits of the mothers

The public health nurses interviewed the mothers soon after delivery to establish their smoking habits. Smoking was classified into four categories as current smokers, ever smokers who quit smoking at the start of pregnancy, ever smokers who quit smoking before the pregnancy, and never smokers. In addition, in order to establish their status as passive smokers, participants were asked whether they shared their home with anyone who was currently a regular smoker. We also analyzed the association between passive smoking and dioxin levels in milk among never smokers.

2.3. Statistical analysis

Because of the skewed distribution of dioxins in human milk, we analyzed log transformed values of PCDDs, PCDFs, the sum of PCDDs and PCDFs (PCDDs + PCDFs), dioxin-like PCBs, and the total of these compounds (total dioxins), and calculated the geometric means of these compounds. First, we compared these dioxins in human milk among the four categories of smoking habits by using one-way analysis of variance (ANOVA). The Bonferroni method was used to compare the dioxin levels between two groups among those four categories. Next, we also compared dioxins among the same categories by age of primiparas because the age of mother was considered to be a confounding factor. We divided the primiparas into two groups: women aged 29 years or younger, and those aged 30 years or older. Finally, the age related dioxin content of breast milk was compared between two groups of mothers who were never smokers, one group being exposed to passive smoking and the other not. Probabilities less than 0.05 were considered to be statistically significant. These statistical analyses were performed by using SPSS® 11.0J for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

The total number of participants in the human milk survey from 1998 through 2004 was 963. We excluded both mothers whose levels of dioxins in their milk could not be measured ($n = 5$) and secundiparas ($n = 105$) from the total number of participants, therefore, 853 primiparas were analyzed. The numbers of current smokers, ever smokers who quit smoking at the pregnancy, ever smokers who quit smoking before the pregnancy, and never smokers by age of mothers are shown in Table 1. The prevalence of current smokers, ever smokers, and never smokers among all the primiparas was 3.9%, 25.7%, and 70.0%, respectively.

When we compared the means of log transformed values of dioxins among the four smoking habit groups, all the differences in PCDDs, PCDFs, PCDDs + PCDFs, dioxin-like PCBs, and total dioxins were statistically significant (ANOVA, $p < 0.001$). The geometric mean of dioxin-like PCBs in the milk of never smokers was the highest among the four categories of smoking habits (9.2 pg TEQ/g fat); followed by ever smokers who quit smoking before the pregnancy, ever smokers who quit smoking at the pregnancy, and current smokers (7.5, 7.2, and 6.6 pg TEQ/g fat, respectively) (Fig. 1). In comparison to the means of log transformed values between two groups among the four smoking habit groups, the differences in the levels of dioxin-like PCBs between never smokers and other smoking habit groups were statistically significant. Regarding PCDDs and PCDDs + PCDFs, the differences between never smokers and the two groups of ever smokers were statistically significant; however, the difference between never smokers and current smokers was not significant

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Table 1
Number of participants by age and smoking habits of mothers

Age of mothers	*n* (%)					
	Current smokers	Ever smokers 1[a]	Ever smokers 2[b]	Never smokers	*n/a*[c]	Total
20–29 years old	22 (4.9)	87 (19.4)	30 (6.7)	307 (68.5)	2 (0.4)	448 (100)
30–39 years old	11 (2.7)	64 (15.8)	38 (9.4)	290 (71.6)	2 (0.5)	405 (100)
Total	33 (3.9)	151 (17.7)	68 (8.0)	597 (70.0)	4 (0.5)	853 (100)

[a] Ever smokers who quit smoking at the pregnancy.
[b] Ever smokers who quit smoking before the pregnancy.
[c] No answer.

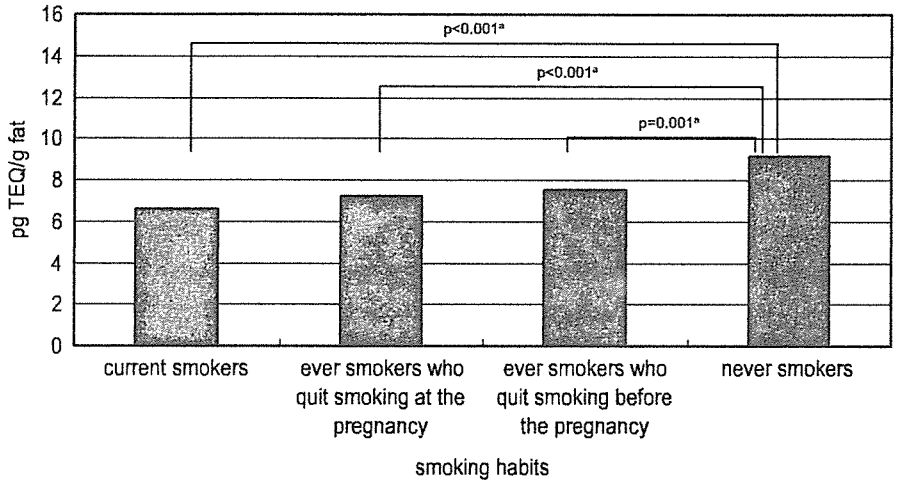

Fig. 1. The geometric means of dioxin-like PCBs (TEQ) in human milk in relation to the smoking habits of primiparas. [a]Bonferroni method.

($p = 1.00$) (Fig. 2). The difference in PCDFs only between never smokers and ever smokers who quit smoking at the pregnancy was significant. In terms of total dioxins, the differences between never smokers and other smoking habit groups were significant; however, the geometric mean of current smokers was not the lowest.

The differences in the means of log transformed values of PCDDs, PCDFs, PCDDs + PCDFs, dioxin-like PCBs,

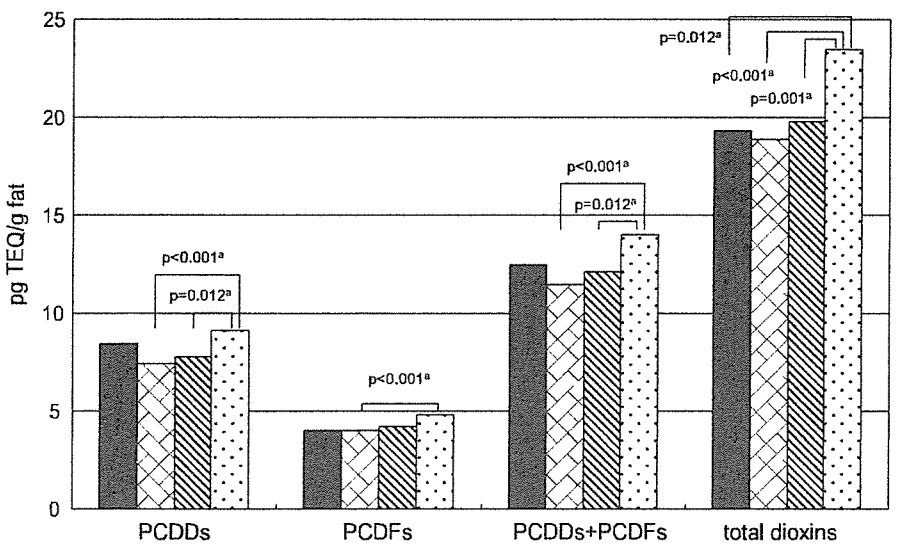

Fig. 2. The geometric means of PCDDs, PCDFs, PCDDs + PCDFs, and total dioxins (PCDDs + PCDFs + dioxin-like PCBs: TEQ) in human milk in relation to the smoking habits of primiparas. Black bar represents current smokers. Cross-hatched bar represents ever smokers who quit smoking at the pregnancy. Oblique-lined bar represents ever smokers who quit smoking before pregnancy. Dotted bar represents never smokers. [a]Bonferroni method.

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and total dioxins among the four categories of smoking habits compared by age of the mothers were also statistically significant (ANOVA). In terms of dioxin-like PCBs, never smokers among both mothers aged 29 years or younger and mothers aged 30 years or older had the highest levels of these compounds; however, the difference between never smokers and current smokers of only mothers aged 30 years or older was significant (Table 2). Although no statistical significance was observed, the levels of all the dioxins and dioxin-like PCBs of current smokers among mothers aged 30 years or older were lower than those of current smokers among mothers aged 29 years or younger. On the other hand, among the other two groups of ever smokers or never smokers, the levels of all the dioxins

Table 2
Comparison between dioxins levels in human milk among four categories of mothers' smoking habits by age

Dioxins (pg TEQ/g fat) age of mothers	Geometric mean (95% confidence interval)				
	Current smokers	Ever smokers 1[a]	Ever smokers 2[b]	Never smokers	p Value[c]
PCDDs					
20–29 years old ($n = 448$)	8.5 (7.3–10.0)	7.1 (6.6–7.7)	7.4 (6.5–8.4)	8.4 (8.1–8.8)	0.001
30–39 years old ($n = 405$)	8.1 (6.4–10.2)	7.9 (7.2–8.7)	8.2 (7.0–9.6)	9.8 (9.4–10.2)	<0.001
PCDFs					
20–29 years old ($n = 448$)	4.2 (3.5–5.0)	3.8 (3.6–4.1)	4.1 (3.4–4.9)	4.5 (4.3–4.7)	0.004
30–39 years old ($n = 405$)	3.8 (3.0–4.8)	4.2 (3.8–4.7)	4.3 (3.8–5.0)	5.1 (4.9–5.4)	<0.001
PCDDs + PCDFs					
20–29 years old ($n = 448$)	12.8 (10.9–14.9)	11.0 (10.3–11.8)	11.6 (10.1–13.3)	13.1 (12.5–13.6)	0.001
30–39 years old ($n = 405$)	12.0 (9.8–14.7)	12.2 (11.1–13.5)	12.6 (10.9–14.5)	15.1 (14.5–15.6)	<0.001
Dioxin-like PCBs					
20–29 years old ($n = 448$)	6.7 (5.4–8.3)	6.6 (6.1–7.1)	6.7 (5.7–7.8)	8.5 (8.1–8.9)	<0.001
30–39 years old ($n = 405$)	6.3 (4.6–8.5)	8.0 (7.2–9.0)	8.3 (7.3–9.4)	10.1 (9.7–10.5)	<0.001
Total dioxins					
20–29 years old ($n = 448$)	19.7 (16.9–23.1)	17.8 (16.7–19.0)	18.5 (16.2–21.2)	21.8 (20.9–22.6)	<0.001
30–39 years old ($n = 405$)	18.6 (14.9–23.2)	20.6 (18.7–22.7)	21.0 (18.4–23.9)	25.4 (24.5–26.3)	<0.001

[a] Ever smokers who quit smoking at the pregnancy.
[b] Ever smokers who quit smoking before the pregnancy.
[c] One way analysis of variance (ANOVA).

Table 3
Relation between dioxins levels in human milk among never smokers and passive smoking habits by age

Dioxins (pg TEQ/g fat) age of mothers	Passive smoke				
	Yes		No		p Value[a]
	Geomertic mean	Mean of log transformation	Geomertic mean	Mean of log transformation	
PCDDs					
20–29 years old ($n = 307$)	8.8	2.18	8.2	2.10	0.10
30–39 years old ($n = 290$)	9.7	2.27	9.9	2.29	0.56
All mothers ($n = 597$)	9.2	2.22	9.0	2.20	0.38
PCDFs					
20–29 years old ($n = 307$)	4.6	1.53	4.5	1.50	0.56
30–39 years old ($n = 290$)	5.0	1.60	5.2	1.66	0.26
All mothers ($n = 597$)	4.8	1.57	4.8	1.58	0.76
PCDDs + PCDFs					
20–29 years old ($n = 307$)	13.5	2.61	12.8	2.55	0.18
30–39 years old ($n = 290$)	14.7	2.69	15.3	2.73	0.35
All mothers ($n = 597$)	14.1	2.65	13.9	2.63	0.66
Dioxin-like PCBs					
20–29 years old ($n = 307$)	9.0	2.19	8.2	2.10	0.05
30–39 years old ($n = 290$)	10.0	2.30	10.2	2.30	0.56
All mothers ($n = 597$)	9.4	2.25	9.1	2.21	0.27
Total dioxins					
20–29 years old ($n = 307$)	22.7	3.12	21.2	3.06	0.10
30–39 years old ($n = 290$)	24.9	3.21	25.7	3.20	0.37
All mothers ($n = 597$)	23.7	3.17	23.3	3.15	0.51

[a] The results from comparison with means of log transformation of dioxins levels by t test.

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and dioxin-like PCBs in mothers aged 30 years or older tended to be higher than those in mothers aged 29 years or younger.

The number of never smoking mothers with passive smoking status was 237. When compared with the means of log transformed values of PCDDs, PCDFs, PCDDs + PCDFs, dioxin-like PCBs, and total dioxins in the milk of never smokers who were not exposed to passive smoking, those of never smokers who were exposed to passive smoking were not significantly different (Table 3). Similar results were obtained when the age related dioxin levels in mothers who were exposed to passive smoking were compared to those in mothers who had negative passive smoking status.

4. Discussion

The levels of dioxins, especially dioxin-like PCBs, in human breast milk of primiparas were associated with cigarette smoking. The levels of dioxin-like PCBs in milk were the highest among never smokers followed by ever smokers and current smokers. This association was also observed among mothers aged 30 years or older. Passive smoking by mothers was less likely to affect the levels of dioxins and dioxin-like PCBs in human milk. It is interesting that the levels of all the dioxins and dioxin-like PCBs in mothers aged 30 years or older were lower than those of mothers aged 29 years or younger among current smokers. This finding indicates that cigarette smoking appears to be counteracting the effect of age in the association with the levels of dioxins and dioxin-like PCBs in human milk. Flesch-Janys et al. (1996) showed that some isomers of PCDDs or PCDFs in the blood of smokers decayed significantly faster than those in the blood of non-smokers and ex-smokers. They suggested that cigarette smoking might increase the rate of dioxin elimination in humans. In our study, the levels of dioxins and dioxin-like PCBs in the milk of never smokers were the highest among the four categories of smoking habits. The differences in the levels of dioxin-like PCBs between never smokers and the other two groups of ever smokers or current smokers were statistically significant. These findings appear to support the hypothesis of Flesch-Janys et al. (1996). In addition, it may be hypothesized that the elimination of dioxins due to cigarette smoking would be enhanced in older mothers.

To determine the relationship between the duration of the smoking-free period before pregnancy and the levels of dioxins in breast milk, we divided the ever smokers into two groups: ever smokers who quit smoking at the start of pregnancy and those who quit smoking before the pregnancy. However, the differences in the levels of dioxins and dioxin-like PCBs in the breast milk of the two groups of ever smokers were not significant. Among ever smokers, the duration of the smoking-free period until pregnancy was not associated with the levels of dioxins and dioxin-like PCBs in breast milk. When compared with the levels of dioxins in the milk of never smokers who were not exposed to passive smoking, those of never smokers exposed to passive smoking were not significantly different. On the other hand, Fürst et al. (1992) reported that the levels of PCDDs and PCDFs in the milk of mothers exposed to passive smoking were significantly lower than those of non-exposed mothers. Further studies relating passive smoking to dioxin levels in human milk will be needed since there is currently a paucity of such studies.

We had to consider several limitations of this study. First, we obtained information regarding the smoking habits of participants by interview and participants may have been tempted to answer incorrectly because of negative attitudes towards smoking during pregnancy. The prevalence of current smokers aged 29 years or younger in our study was 4.9%, which was smaller than the prevalence reported in Sweden (Cnattingius, 2004) and in another cohort in Japan (Tanaka et al., 2005). Even if this information bias remained, however, it probably underestimated the relationship between smoking habits of mothers and levels of dioxins in breast milk. Next, among the four categories of smoking habits, current smokers had the lowest levels of dioxin-like PCBs; however, the differences between current smokers and the other two groups of ever smokers were not statistically significant. The small sample size of the current smokers may have influenced this result. Finally, we did not collect biochemical markers related to cigarette smoking, for example, cotinine concentration in the urine of mothers. The measurement of these markers as well as smoking habits may significantly clarify the relationship between cigarette smoking and dioxins levels in human breast milk.

In conclusion, the levels of dioxin-like PCBs in human milk were negatively related to the smoking habits of the mothers; in addition, the age of the mothers affected this relationship. We speculate that cigarette smoking may induce some biological mechanisms for the elimination of dioxins from the human body.

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Human milk survey for dioxins in the general population in Japan

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Abstract

Background: Much attention has been paid to the level of dioxins in breast milk in Japan but few large-scale studies have been conducted on the subject.

Methods: From 1997 to 2002, we collected 839 samples of breast milk from primiparas residing throughout Japan. Starting in 1999, breast milk was also collected from secundiparas. Seven isomers of polychlorinated dibenzo-*p*-dioxins (PCDDs), 10 of polychlorinated dibenzofurans (PCDFs), 4 of coplanar polychlorinated biphenyls (Co-PCBs) and 8 of mono-orthochlorinated polychlorinated biphenyls (mono-ortho PCBs) were analyzed by employing gas chromatography and mass spectrometry. A correlation between the level of dioxins in human milk and the age of the mothers was noted for the primiparas and the secundiparas; and the levels were compared between the first and the second deliveries. Grouped by parity and prefecture in each year, observations were also made on the trends in these levels. Dioxin levels are shown by using geometric means because their distributions were skewed to the left.

Results: The sum of PCDDs and PCDFs, Co-PCBs, mono-ortho PCBs, and total dioxins in the breast milk of primiparas were 13.9, 5.4, 3.4, and 22.7 pg TEQ/g fat, respectively. In the samples obtained from secundiparas, these levels were 63–68 percents of those taken from the primiparas. The correlation coefficients between the PCDDs/DFs, Co-PCBs, mono-ortho PCBs, and total dioxins and the age of the primiparas were 0.19, 0.17, 0.36, and 0.24, respectively. All these correlations were statistically significant ($p < 0.001$). The positive correlations between these contaminants and the age of the secundiparas were also examined. The total dioxins as well as PCDDs/DFs, Co-PCBs, and mono-ortho PCBs in the breast milk of the primiparas declined significantly between 1998 and 2002 (regression coefficients: −0.04, −0.05, −0.03, and −0.03, respectively). However, no significant decline in these levels was observed when sorted by prefectures.

Conclusions: Much attention should be paid to the age and parity of nursing mothers when investigating the relationship between the level of dioxins in breast milk and the body burden of infants.

Keywords: Dioxins; Polychlorinated biphenyls; Human milk; Epidemiology; Population surveillance

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1. Introduction

The toxicity of dioxins such as polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) is extremely high and their effects on reproductive systems, thyroid function, the immune system, and development in some animal models are significant (Yonemoto, 2000). In humans, however, it is controversial whether reproductive and hormonal systems and the developmental mechanism are affected by these contaminants (Yonemoto, 2000; Matsuura et al., 2001; Vreugdenhil et al., 2002). The effects of exposure to dioxins are most prominent in fetuses and infants; therefore studies have focused on this segment of the population.

Food intake, inhalation of polluted air and skin contact with contaminated soil and materials are possible routes of human exposure (Watanabe et al., 1999). It is estimated that for the general population in Japan, most dioxins originate in food, primarily fish and meat. For the majority of infants, breast milk is the most important source of their nutrition and immunologically active substances. Because breast milk is rich in fat and dioxins are highly lipophilic, consumption of breast milk constitutes the main route of dioxin exposure for breast-fed infants. The dioxin content in human breast milk has been measured in Japan and western countries (Iida et al., 1999; Nakagawa et al., 1999; Tajimi et al., 2004; Takekuma et al., 2004). However, few large-scale studies have been conducted and sampling of breast milk was limited geographically in earlier studies. For the current study, starting in 1997, samples of human breast milk was measured throughout Japan and the levels of dioxins in these samples were measured. Thus the pattern of distribution of the dioxin levels in breast milk in this country was observed and described from the viewpoints of time and geography.

2. Methods

In 1997, 20 primiparas each from four prefectures (Saitama, Tokyo, Ishikawa and Osaka) were enrolled; and in 1998, the same number of primiparas from 19 prefectures (Iwate, Miyagi, Akita, Ibaragi, Gunma, Chiba, Kanagawa, Niigata, Ishikawa, Yamanashi, Shizuoka, Aichi, Osaka, Shimane, Hiroshima, Yamaguchi, Fukuoka, Kumamoto and Okinawa) and Yokohama City were enrolled (Fig. 1). Starting in 1999, the same numbers of new primiparas from six prefectures (Iwate, Chiba, Niigata, Ishikawa, Osaka and Shimane) were enrolled. There are 47 prefectures in Japan and all were invited to participate in this study but no response was received from other prefectures. When 20- to 39-year-old healthy pregnant women visited their obstetricians, they were asked by the public health nurses in their

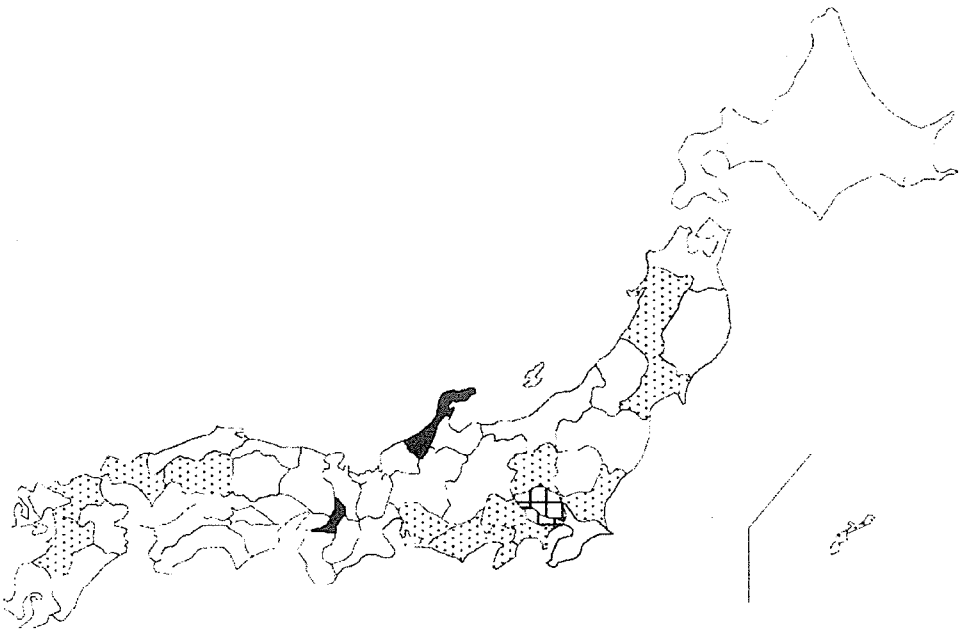

Fig. 1. Title: The map of prefectures in Japan that participated in our study from 1997 to 2002. Crosses represent ones that participated in our study in 1997 (Saitama and Tokyo). Dots represent prefectures and a city that participated in 1998 (Miyagi, Akita, Ibaragi, Gunma, Kanagawa, Yamanashi, Shizuoka, Aichi, Hiroshima, Yamaguchi, Fukuoka, Kumamoto, Okinawa, and Yokohama City). Blacks represent ones that participated from 1997 to 2002 (Ishikawa and Osaka). Grays represent ones that participated from 1998 to 2002 (Iwate, Chiba, Niigata, and Shimane).