Abstract: The Objective of this study was to elucidate if Bisphenol A (BPA) administration modulates T helper (Th) cell component of immune responses in a mouse challenged with ovalbumin (OVA), a major food antigen. BALB/c mice, (6 weeks old, female) were orally given either OVA (OVA-fed) or water (Water-fed), immunized intraperitoneally with OVA and injected with either BPA in corn oil or the vehicle alone. After subsequent 2nd immunization, serum titers of total IgE, OVA-specific IgE, IgG, IgG1 IgG2a and ability of their splenocytes for production of interferon (IFN)-γ, interleukin (IL)-4 and IL-12 were examined by ELISA. Lymphocyte proliferation assay against concanavalin A (Con A) or OVA was also performed for 3H-Thymidine incorporation.

In Water-fed groups, treatment with BPA resulted in lower titers of total IgE ($P<0.01$) and higher levels IgG2a ($P<0.05$) followed by a higher IFN-γ ($P<0.05$) and IL-12 ($P<0.05$) with an intact IL-4. When OVA-fed groups were examined, the compound did not change production of total and OVA-specific IgE and -IgG2a but resulted in lower production of IFN-γ ($P<0.05$). Also, BPA resulted in impaired lymphocyte proliferation to Con A in Water-fed groups ($P<0.05$) but not in tolerated animals. The findings indicate that BPA results in augmentation of Th1 immune responses but no significant effect on an established tolerance to OVA. J. Med. Invest. 53: 70-80, February, 2006

Keywords: BPA, food allergy, OVA, IgE, IgG2 t cytokines
Animals, diets and husbandry

A total of 24 animals, 12 females and 12 males, were divided into 3 groups. The first group of animals was fed a diet containing 200 mg of antigen per kilogram of diet (AG1). The second group was fed a diet containing 670 mg of antigen per kilogram of diet (AG2). The third group was fed a diet containing 50 mg of antigen per kilogram of diet (AG3). All animals were fed ad libitum.

Table 1: Diet composition

<table>
<thead>
<tr>
<th>Protein Source</th>
<th>Amount (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casein</td>
<td>200</td>
</tr>
<tr>
<td>Casein</td>
<td>670</td>
</tr>
<tr>
<td>Casein</td>
<td>50</td>
</tr>
</tbody>
</table>

Experimental design for Induction of oral tolerance and immunization

The animals were fed the respective diets for a period of one month. During this time, the animals were observed for any signs of behavioral changes or disease. At the end of the one-month period, the animals were sacrificed and the gut was removed for further analysis. The gut was fixed in formalin and then embedded in paraffin for histological examination.

1. [Footnote information]
2. [Footnote information]
3. [Footnote information]

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Administration of BPA

Preparation of Blood serum and Spleen cell suspension

Measurement of Total and OVA-specific IgE
Measurement of OVA specific IgG, IgG1 and IgG2a in Serum

Cytokine Production

Lymphocyte Proliferation Assay
Effects of BPA on total and OVA-specific IgE

Effect of BPA on OVA-specific IgG, -IgG1 and -IgG2a

Effects of BPA on cytokine production

Effect of BPA on OVA-specific IgG, -IgG1 and -IgG2a

Effects of BPA on cytokine production
Effects of BPA on lymphocyte proliferation

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Effects of BPA on lymphocyte proliferation

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![Graph A: IgG Absorbance vs. Water-fed vs. OVA-fed](image1)

![Graph B: IgG1 Absorbance vs. Water-fed vs. OVA-fed](image2)

![Graph C: IgG2a Absorbance vs. Water-fed vs. OVA-fed](image3)
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Effect of Bisphenol A on immune responses

![Graph A](image1.png)

![Graph B](image2.png)

![Graph C](image3.png)
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Effect of Bisphenol A on immune responses