Clinical observation of acute delayed neurotoxicity study for 21 days of organophosphate using triorthocresyl phosphate (TOCP) as a model for organophosphate neurotoxicity, adult hens were dosed by oral gavage with 500 mg/kg/bw single dose. Treated hens showed varying degrees of in-coordination, ataxia and paralysis at varying grades and on varying days of treatment mostly depending on the various metabolisms of the neurotoxic compound by the individual bird. Aggrading was suggested reflecting the severity of the effect on different hens and that was from 1 to 6, therefore birds with slight in-coordination were considered to be 1 to 2, those with ataxia were considered to be 3 to 4 and those with paralysis were considered 5 to 6. Some birds with the paralysis died because of starvation as they could not feed themselves.

**KEYWORDS:** Tri- Ortho Cresyl Phosphate, Clinical and Hen.

**INTRODUCTION**

This review describes a group of organophosphorus compounds with delayed neurotoxic properties [1]. Delayed neurotoxicity is a delayed onset of pro-longed loco motor ataxia resulting from a single or repeated exposure to an organophosphorus compound [2, 3]. In animals as well as man, there is a latent period between exposure and manifestations of OPIDN. The domestic chicken (hen) is the recognized animal model for OPIDN[4]. Effects on the legs are noted, and the hen exhibits progressive incoordination and difficulty in walking. Eventually ability to walk is lost and the wings, too, become involved. There is an age-related susceptibility, in that these effects are not seen in chickens less than 55 d of age. Progressive ataxia is also seen in adults of other susceptible species (e.g., cats, sheep, water buffalo, horses, ferrets). Ataxia has not been a prominent feature of OPIDN in rodents [5]. Signs of neurologic deficits produced by delayed neurotoxic organophospho-
rus compounds depend on both the type of compound and animal species. Although clinical
signs for Types I and II OPIDN were indistinguishable quantitatively in the adult chicken [6],
other species exhibited distinct
signs characteristic of each syndrome. Chickens treated with large oral doses of aryl
phosphites exhibited signs of acute effect within 3 hours of dosing [7]. These signs were
characterized by tremors, somnolence (drowsiness), dyspnea (labored breathing), and leg
weakness. Large oral doses of TOCP produced acute cholinergic effect in chickens including
diarrhea, salivation, and leg weakness [8]. Chickens that survive acute toxicity usually
recover within three days of dosing. (b) Delayed neurotoxicity: Although TPPi and TOCPj
produced delayed neurotoxicity in chickens, TMCPj and TPCPj did not [6].
Chickens treated with TPPi or TOCPi developed ataxia 4-5 days after dosing. The condition
of the chickens progressed to flaccid leg paralysis 10-12 days after dosing [9]. TOCP and
other Type I compounds produce ataxia and flaccid paralysis in chickens that are
indistinguishable from those produced by Type II com-pounds (I). The only difference is in
the time onset of clinical signs; Type I compounds produced clinical signs of OPIDN a few
days later than Type II.

MATERIALS AND METHODS
Experimental design
Twenty adult hen of over six months old were divided in two groups, 10 untreated control
and 10 treated, the treatment was control dosed orally by corn oil but the treated ones were
dosed orally with 500 mg/kg of TOCP in corn oil in single dose and the bird were left for 21
days for observation after that were killed.
In case of subchronic for 90 days, birds were dosed orally the same with TOCP in corn oil as
5mg/kg per day as high dose, 2.5mg/kg per day as intermediate dose and 1.75mg/kg per day
as low dose.

RESULTS
Clinical study of hens intoxicated with neurotoxic of tri ortho cresyl phosphate(TOCP)
showed grade1,note the bird with early signs of ataxia as in (fig1), while in grade 2 showed
ataxia, note the bird lying on its hooks(fig2). furthermore some birds showed in grade 3 with
ataxia lying on its hooks with mild signs of salivation (fig3), some bird with ataxia grade 4
lying on its hooks, note signs of gasping in (fig 4,fig 5). In addition in (fig 6) bird with
paralysis, of grade 5, ruffled feathers and mark signs of gasping. Paralysis, grade 6, curled toe unable to move and gasping (fig7). The bird with normal limits in (fig 8)

Fig 1: Adult hen with early signs of ataxia, grade 1.

Fig 2: Adult hen showed grade 2 ataxia note the bird lying on its hooks.

Fig 3: Adult hen showed grade 3 with ataxia lying on its hooks with mild signs of salivation.
DISCUSSION
Clinical observation on neurotoxicity of organophosphorus using tri ortho cresyl phosphate (TOCP) as a model was studied by several author's doing neurotoxicity studies. CATS Cats treated with Type II compounds, e.g. TPPj, TOCPj, TMCPj, and TPCPj,
developed ataxia after 4-26 days, and 2-16 days thereafter developed extensor rigidity of both fore- and hind limbs of relatively long duration [7]. TMCPj produced the least acute cholinergic effects, whereas TPCPj was the most acutely toxic of the four chemicals. Furthermore, aryl phosphate produced a rise in body temperature of cats of 0. 9-2. SoC at onset of ataxia or a day sooner [6]. In contrast, cats treated with EPN [10] or TOCP [11], both of which are Type I compounds, only exhibited flaccid paralysis. MONKEYS Type I and Type II compounds produced effects similar to those in the cat. Monkeys treated with a s.c. dose of 1 mg/kg TPPj in two doses at a 24-day interval, developed ataxia within 12 days of the second dose. Extensor rigidity of the limbs and some retraction of the head developed three days later [6]. On the other hand, TPP, a Type I compound, produced pronounced flaccid paralysis of the posterior extremities 8 days after injection of 500mg/kg [6]. RATS

(a) Acute effects: All four aryl phosphites tested were acutely toxic in the rat after subcutaneous injections: TPPj > TPCPj > TmCPj > TOCPj. Acute effects usually developed within a few hours after dosing in animals that survived. Signs of acute toxicity were reported as generalized tremors involving large muscle groups. Recent studies using Long-Evans rats showed that single or multiple sub-cutaneous doses of TPPj produced tremors within 1 hour of injection, although they subsided within 4-6 hours [12]. These animals became lethargic for 2-3 days. The site of subcutaneous injection exhibited irritation, edema, congestion, ulceration, and occasional necrosis following multiple injections [7]. Rats treated with TOCP developed cholinergic signs such as tremors, lacrimation, and diarrhea 4 days after dosing [13]. Although these signs disappeared with time, the animals appeared slightly hyperactive.

(b) Signs of delayed neurotoxicity: Following treatment with TOCP, neither Long-Evans, Sprague-Dawley, nor Fischer 344 rats exhibited behavioral nor clinical signs of OPION [14, 15]. However, delayed neurotoxicity signs developed a few days after the injection of aryl phosphites (Type II). These signs were hyperexcitability, some spasticity" in coordination, and later partial flaccid paresis of the extremities [6]. TPPj and TOCPj were more effective than TMCPj and TPCPi in producing OPIDN. Smith et al suggested that these signs in the rat were a different manifestation than the extensor rigidity seen in the cat. Recent studies [12] on Long-Evans rats reported that multiple doses of TPPi produced tail-kinking in the proximal one-inch of the tail. These rats developed hind-leg ataxia within one week, followed by paralysis. Furthermore, rats developed circling behavior following multiple doses of TPPj.

CHICKENS

(a) Acute effects: Chickens treated with large oral doses of aryl phosphates exhibited signs of acute effect within 3 hours of dosing [7]. These signs were characterized
by tremors, somnolence (drowsiness), dyspnea (labored breathing), and leg weakness. Large oral doses of TOCP produced acute cholinergic effect in chickens including diarrhea, salivation, and leg weakness [8, 9]. Chickens that survive acute toxicity usually recover within three days of dosing. (b) Delayed neurotoxicity: Although TPPi and TOCPj produced delayed neurotoxicity in chickens, TMCPj and TPCPj did not [6]. Chickens treated with TPPi or TOCPi developed ataxia 4-5 days after dosing. The condition of the chickens progressed to flaccid leg paralysis 10-12 days after dosing [6, 8, 9]. TOCP and other Type I compounds produce ataxia and flaccid paralysis in chickens that are indistinguishable from those produced by Type II compounds (I). The only difference is in the time onset of clinical signs; Type I compounds produced clinical signs of OPIDN a few days later than Type II.

**Research highlights**
This project is concentrated on acute delayed neurotoxicity model using TOCP as the neurotoxic agent.

**Finding and policy aspects**
The findings gives TOCP as a model or positive control to study neurotoxicity of different insecticides and any other compound to check if any effect on the nervous system as a primary or secondary toxic target.

**Justification of research**
Being the nervous system the most important system in the body, therefore study of effect of any compound on the nervous system is priority with TOCP as positive control. From the above point of as the neurotoxicity is very important from the health point of view for any compound.

**Conclusion**
The present study showed that TOCP is very good model for neurotoxicity as positive control of any compound previous and new.

**Recommendation**
The present research indicates that the TOCP is the best model for neurotoxicity.
REFERENCES