INTRODUCTION
Persistent corneal epithelial defects (PED) can be caused by several definite etiologies like dry eyes, corneal limbal stem cell deficiency, diabetes, post-herpetic neurotrophic disorders and chronic graft versus host disease (cGVHD). Conventional therapy includes treatment of underlying cause, lubrication of ocular surface with artificial tears, topical antibiotics and use of bandage contact lenses. Autologous serum eye drops are a new therapeutic modality for treatment of PED which are unresponsive to conventional therapy. Serum has got biochemical properties similar to natural tears and is thus tolerated well. Human serum contains various substances such as epidermal growth factor (EGF), vitamin A, transforming growth factor β (TGF β), fibronectin and cytokines which are normally present in tears. These factors play a vital role in maintenance of a healthy corneal and conjunctival epithelium.

The purpose of this research was to study a minimally invasive modality of treatment in patients of PED, so that their corneal defect can be healed earlier.

METHODOLOGY
The study was conducted at the Armed Forces Institute of Ophthalmology (AFIO), Rawalpindi, from September 2009 till February 2012 including the follow-up time. Inclusion criteria included patients older than 12 years of age and having PED. Exclusion criteria included those corneal epithelial defects classified as progressive corneal melting caused by rheumatoid process or Mooren’s ulceration. Patients with active microbiol infection, acute herpetic eye disease, drug toxicity, or recurrent corneal erosion syndrome were also excluded from study. PED was defined as persistent corneal epithelial defects of minimum 2 weeks duration in which conventional therapy had failed. Conventional therapy was defined as artificial tears, topical antibiotics and bandage contact lenses.

Patients of PED were selected from outpatient depart- ment by convenient sampling procedure. Informed consent was taken from all patients. They were given ID, their age, gender primary diagnosis, previous treatment modality, duration and size of PED was noted. Schirmer test without anaesthesia was performed and a value less than 10 mm was taken as significant. Then they were prescribed with 100% autologous serum eye drops to be used on hourly basis during waking hours, while rest of all medications were discontinued. Patients were examined before treatment and then daily for next two weeks. Then they were examined on weekly basis until serum eye drops were stopped. They were then followed-up on 6 weekly intervals for next 18 months to document any recurrence of PED after healing.

Autologous serum drops were dispensed as follows: Venesection was performed at the cubital fossa under strict aseptic conditions. Twenty ml of blood was collected into sterile container. Blood was left standing for 2 hours at room temperature to allow clotting to take place. Blood was centrifuged at 3000 revolution per minute for 15 minutes. Serum was carefully separated in a sterile manner and put in bottles with ultraviolet light
cut coating. As vitamin A is easily degraded by light, patients were instructed to keep bottle in refrigerator at +4°C. Shelf life of serum drops are 01 month in refrigerator at +4°C.1

Serum eye drops were evaluated as 'effective' when epithelial defect healed within 2 weeks. When the defect did not heal completely within 2 weeks but had shown a tendency to heal in 2 weeks time and healed completely in 01 month, it was labeled as 'partially effective'. When healing required more than 1 month, the treatment was considered as 'ineffective', serum drops were stopped and surgical intervention was carried out in those patients.1

Statistical Package for Social Sciences (SPSS) version 10.0 was used to analyze the data. Mean of age, duration of PED and duration of healing in 'effective' cases were calculated. Male to female ratio and percentage of success was also calculated.

RESULTS
Mean age of patients was 43.4 years. There were 06 male and 04 female patients in the study with male to female ratio of 3:2. Mean duration of PED before treatment was 37.2 days and mean duration of healing in case of effective treatment was 4.8 days. The success rate was 80%. Seven patients had effective treatment in which healing occurred within 2 weeks. Only one case was partially effective that had healed at day 20. In 2 cases, healing did not occur even at 01 month and temporary tarsorrhaphy was performed in both cases. There was no case with secondary infection or recurrence of PED. The detail of all patients is summarized in Table I.

DISCUSSION
This series of 10 patients has supported the previous work done on autologous serum for PED that had shown favourable results. Tsubota et al. evaluated efficacy of autologous serum in 16 eyes of 15 patients with PED.1 He reported success rate of 43.8% within 2 weeks and 62.5% within 1 month with no apparent side effects. He used 20% autologous serum 6 – 8 times a day in addition to frequent use of preservative free artificial tears and highly viscous hyaluronic acid 4 times a day along with special dry eye glasses while we used 100% autologous serum on hourly basis during waking hour and stopped all other modalities. This study proved that use of pure autologous serum is more effective (43.8% vs. 70%) at 2 weeks. The most probable cause of better results in this study is 5 times greater amount of essential tear components like EGF, vitamin A and TGF-β1 necessary for wound healing process of corneal epithelium.

Young et al. in his study of 10 patients revealed success rate of 60% at 2 weeks.7 He used 20% serum 6 – 14 times a day in addition to bandage contact lens in one patient, lateral tarsorraphy in 3 patients and amniotic membrane transplant (AMT) in 5 patients. In another

### Table I: Summary of clinical details for PED patients.

<table>
<thead>
<tr>
<th>Patient ID No.</th>
<th>Eye R/L</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Primary diagnosis</th>
<th>Previous modalities tried</th>
<th>Duration of PED (days)</th>
<th>Size of PED (mm)</th>
<th>Schirmer test &lt;10 mm</th>
<th>Time of healing (days)</th>
<th>Time of cessation of treatment for failure (days)</th>
<th>Outcome</th>
<th>Reason for failure/ remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L</td>
<td>60</td>
<td>F</td>
<td>Post PKP</td>
<td>Artificial tears</td>
<td>60</td>
<td>4 x 3</td>
<td>No</td>
<td>3</td>
<td>Nil</td>
<td>Effective</td>
<td>Nil</td>
</tr>
<tr>
<td>2</td>
<td>R</td>
<td>70</td>
<td>M</td>
<td>Post PKP</td>
<td>Artificial tears</td>
<td>45</td>
<td>3 x 4</td>
<td>No</td>
<td>3</td>
<td>Nil</td>
<td>Effective</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>R</td>
<td>38</td>
<td>M</td>
<td>Post PKP</td>
<td>BCL, Artificial tears</td>
<td>120</td>
<td>4 x 4</td>
<td>No</td>
<td>3</td>
<td>Nil</td>
<td>Effective</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>R</td>
<td>65</td>
<td>M</td>
<td>Neurotrophic HSV</td>
<td>Topical acyclovir, artificial tears</td>
<td>14</td>
<td>4 x 3</td>
<td>No</td>
<td>14</td>
<td>Effective</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>L</td>
<td>75</td>
<td>M</td>
<td>Neurotrophic HSV</td>
<td>Topical acyclovir, artificial tears</td>
<td>15</td>
<td>3 x 4</td>
<td>No</td>
<td>Non healing till 1 month</td>
<td>1 month</td>
<td>Ineffective</td>
<td>Non-compliance, very slow progress, Tarsorrhaphy done</td>
</tr>
<tr>
<td>6</td>
<td>L</td>
<td>28</td>
<td>F</td>
<td>Post adenoviral keratitis</td>
<td>Topical artificial tears</td>
<td>14</td>
<td>2 x 2</td>
<td>No</td>
<td>2</td>
<td>Nil</td>
<td>Effective</td>
<td>Nil</td>
</tr>
<tr>
<td>7</td>
<td>R</td>
<td>35</td>
<td>F</td>
<td>Sjögren syndrome + dry eye</td>
<td>Topical artificial tears</td>
<td>30</td>
<td>2 x 1</td>
<td>Yes</td>
<td>20</td>
<td>Nil</td>
<td>Partially effective</td>
<td>Nil</td>
</tr>
<tr>
<td>8</td>
<td>L</td>
<td>29</td>
<td>M</td>
<td>Dry eye</td>
<td>Topical artificial tears</td>
<td>20</td>
<td>1 x 1</td>
<td>Yes</td>
<td>4</td>
<td>Nil</td>
<td>Effective</td>
<td>Nil</td>
</tr>
<tr>
<td>9</td>
<td>R</td>
<td>22</td>
<td>M</td>
<td>cGVHD + dry eye</td>
<td>Topical artificial tears</td>
<td>14</td>
<td>4 x 6</td>
<td>Yes</td>
<td>5</td>
<td>Nil</td>
<td>Effective</td>
<td>Nil</td>
</tr>
<tr>
<td>10</td>
<td>L</td>
<td>12</td>
<td>F</td>
<td>VKC</td>
<td>BCL+ mild steroid + antibiotics</td>
<td>40</td>
<td>1 x 1</td>
<td>No</td>
<td>Non healing till 1 month</td>
<td>2 months</td>
<td>Ineffective</td>
<td>Formation of slough over PED, repeated removal done but PED did not heal till 1 month</td>
</tr>
</tbody>
</table>

**Keys:** M = male, F = female, R = right eye, L = left eye, PKP = penetrating keratoplasty, BCL = bandage contact lens, HSV = herpes simplex virus, VKC = vernal keratoconjunctivitis, cGVHD = chronic graft versus host disease.
study conducted by Mirza et al. in Pakistan, success rate of 52.9% was reported at 2 weeks and 70.6% at 1 month. They used 20% autologous serum eye drops in 17 eyes of 10 patients with PED. The present study had shown better results with 70% success rate at 2 weeks. Shakir reported a success rate of 81.8% in healing of PED after AMT over the cornea. Human amniotic membrane produces various growth factors which stimulate epithelization and can act as promoters of epithelization. The present study revealed similar results with minimally invasive methodology. AMT can, therefore, be kept as a second line treatment for non-responders. A young patient of dry eye secondary to cGVHD had Schirmer test of 5 mm wetting also showed success when his defect has healed in just 5 days of therapy. PED is a known but rare manifestation of cGVHD and 75% of these patients have co-existing dry eyes.

**CONCLUSION**

Autologous serum eye drops proved to be an effective, safe and minimally invasive modality of treating PED. It can be used as a sole treatment. Better healing of PED may be related to lesser duration of PED before the start of therapy.

**REFERENCES**