pared with 32% if the tumors undergo biopsy before removal. Rupture of the capsule of a PALG affects the prognosis adversely because of seeding of tumor cells into the surrounding tissues and malignant transformation.7

The etiology of PALG is unknown.

Our patient was initially seen in a condition of first remission 10 years after B-cell−type ALL. At 4 years of age, she received chemotherapy that included daunorubicin, doxorubicin, cyclophosphamide, and methotrexate. Cranial irradiation (1200 rad) was given for prophylaxis of the central nervous system.

The treatment of children with ALL is increasingly successful, with a current overall survival rate of almost 80%. However, the immunosuppressive and cytotoxic therapy necessary to achieve this improvement increases the risk of subsequent complications. There is a 14-fold increase in the incidence of secondary neoplasms after therapy for ALL. The cumulative risk of secondary neoplasms in first complete remission ranges from 1.9% to 2.9% by 15 to 20 years.8,9

The literature contains no report of an association between chemotherapy or irradiation and the incidence of PALG. However, there is evidence that salivary gland tumors can be caused by therapeutic irradiation of the head in childhood, with a long latency and in a dose-response manner.10,11 A 2.6-fold incidence of benign mixed tumors (pleomorphic adenomas) or a 4.5-fold incidence of malignant neoplasia of the salivary gland was noted in a cohort of patients who received 350-rad irradiation of the head for tinea capitis in childhood.12

It is therefore possible that the development of PALG, which shows clinical and histological similarity to the salivary gland tumors mentioned in the preceding paragraph, was influenced by irradiation and chemotherapy for ALL in our case.

The increasing number of children surviving ALL indicates a need for awareness of such neoplasms (which were previously considered to be very rare), comprehensive examination, and long-term follow-up.

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Reversible Changes in Frequency-Doubling Perimetry With Transiently Elevated Intraocular Pressure

Frequency-doubling technology (FDT) has been useful in screening patients for glaucoma.1 One report shows that 1 drop of unoprostone could induce improvement with FDT by lowering intraocular pressure and increasing ocular blood flow.2 We examined 1 patient with secondary glaucoma and transient rise of high intraocular pressure with FDT and with a Humphrey field analyzer (HFA). (Carl Zeiss Meditec, Inc, Dublin, Calif) for 1 year to study the effect of intraocular pressure on visual field results.

Report of a Case. A 33-year-old woman had had attacks of high intraocular pressure with slight inflammation several times in both eyes. Her visual acuity was 20/16.7 OU. Fluorescein angiography showed no abnormal findings. With maximally tolerated therapy, intraocular pressure remained higher than 40 mm HG, and the patient underwent trabeculectomy in that eye. Her left intraocular pressure stayed in the 20s after surgery. Her right intraocular pressure transiently rose to higher than 40 mm Hg with maximally tolerated therapy. The high pressure decreased to normal levels within 1 month. The patient had large disc cupping in the right eye; a 0.472 cup-disc ratio was determined using a retina tomograph (Heidelberg Engineering, Heidelberg, Germany). The HFA visual fields were always normal independent of intraocular pressure for 1 year (Figure 1) (Table). The FDT, however, showed abnormal areas only twice during the same period, with high intraocular pressure (> 40 mm Hg) (Figure 2). On the same day in February 2002, when intraocular pressure was 45 mm Hg, the FDT showed abnormal findings while the HFA appeared normal. During the final attack, 1% apraclonidine reduced intraocular pressure transiently and improved the FDT mean deviation slightly in 1 hour (Figure 2). The FDT mean deviation correlated well with changes in the intraocular pressure, but not necessarily with the FDT pattern standard deviation (Table). No inflammatory cells were seen in the anterior chamber of the right eye and no corneal edema was observed during the attacks.
Comment. In this patient, visual field defects detected with FDT were thought to be due to elevated intraocular pressure. After reduction of intraocular pressure, the FDT mean deviation always showed improvement, even in 1 hour. Visual field loss with FDT under high intraocular pressure was reversible. The mechanism for this improvement was unclear. The FDT was thought to reflect the function of relatively...

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Figure 1. The Humphrey field analyzer always showed normal visual field findings independent of intraocular pressure at examination. MD indicates mean deviation; PSD, pattern standard deviation; CSPD, corrected pattern standard deviation.
large retinal ganglion cells, called the M ganglion cells, since the FDT has large-sized (10°), high-temporal-frequency (25 Hz) and low-spatial-frequency (0.25 candela/s) stimuli, inducing frequency-doubling illusion. The large retinal ganglion cells that may not be completely damaged under elevated intraocular pressure could recover when intraocular pressure was lowered. Another mechanism was improvement in corneal edema. No epithelial edema

<table>
<thead>
<tr>
<th>Visual Field Indexes</th>
<th>No.</th>
<th>$r^2$</th>
<th>$P$ Value†</th>
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</thead>
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<tr>
<td>FDT MD</td>
<td>10</td>
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<td>.04</td>
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<tr>
<td>FDT PSD</td>
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<td>.14</td>
</tr>
<tr>
<td>HFA MD</td>
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<td>.42</td>
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<tr>
<td>HFA CPSD</td>
<td>4</td>
<td>0.002</td>
<td>.96</td>
</tr>
</tbody>
</table>

Abbreviations: CPSD, corrected pattern standard deviation; FDT, frequency doubling technology; HFA, Humphrey field analyzer; MD, mean deviation; PSD, pattern standard deviation.

*Simple regression analysis was done for the relationship.
†$P$ value $/H0.05$ was considered significant.

Figure 2. The frequency-doubling technology (FDT) showed abnormal areas only with high intraocular pressure (> 40 mm Hg) twice and normal visual fields with normal intraocular pressure 6 times. In April 2003, 1% apraclonidine eyedrops decreased intraocular pressure (from 39 to 27 mm Hg) and improved mean deviation (MD) with FDT under the same-sized pupil (6 mm). PSD indicates pattern standard deviation.
was seen by slitlamp microscopy. Not only did diffuse loss mean deviation appear, but abnormal areas appeared with high intraocular pressure in the present patient. If corneal edema affected visual field, only diffuse loss would occur. Refractive error was corrected at examination of FDT. Good visual acuity was maintained under high intraocular pressure. In conclusion, FDT perimetry may show intraocular pressure-dependent, reversible changes.

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Acetazolamide-Induced Thrombocytopenia

Acetazolamide (Diamox; Duramed Pharmaceuticals Inc, Cincinnati, Ohio) is a carbonic anhydrase inhibitor commonly used in ophthalmology to reduce intraocular pressure and to treat some forms of macular edema. Acetazolamide-associated thrombocytopenia was previously described as part of aplastic anemia or other organ involvement; however, evidence that the drug may also cause accelerated platelet destruction has never been provided.1-3 Herein we report an acetazolamide-induced pure thrombocytopenia with the highest level of evidence for a causal relationship of the drug to thrombocytopenia.

Report of a Case. A 67-year-old man who had been receiving metformin for 20 years because of type 2 diabetes mellitus was admitted to our department for cataract surgery. The day after the surgery, intraocular pressure was elevated and 2 daily 250-mg tablets of acetazolamide were prescribed. As the intraocular pressure normalized on day 3, acetazolamide was stopped. A routine blood cell count with examination of the blood smear disclosed an unexpected and isolated thrombocytopenia (platelet count, 31 × 10³/µL) (Figure 1). In the bone marrow, quantitatively and morphologically normal megakaryocytes, including some immature forms, were observed, indicating normal platelet production. Recovery from thrombocytopenia was shown later by ambulatory tests. Drug-induced thrombocytopenia was not suspected.

Eleven months later, acetazolamide (375 mg/d) was prescribed again, this time for macular edema. Two weeks later, the patient developed purpura and was seen in our department a week later. He was hospitalized and found to have a platelet count of 3 × 10³/µL (Figure 2). Acetazolamide, but not metformin, treatment was immediately discontinued. The platelet count rose spontaneously to 20 × 10³/µL the next day, 73 × 10³/µL 3 days later, and 246 × 10³/µL after 10 days. Thrombocytopenia did not recur.

Comment. To our knowledge, acetazolamide-induced thrombocytopenia has been previously reported in only 4 cases.1,3 Moreover, in no case was the causality level high enough to ascertain that the drug was responsible.

As recommended by the American Society of Hematology,4 diagnosis of isolated thrombocytopenia in elderly patients requires bone marrow aspiration to exclude myelodysplasia. In our patient, no bone marrow disorder was found to explain the thrombocytopenia.

Diagnosis of acetazolamide-induced thrombocytopenia was based on positive data including challenge and in vivo rechallenge tests highly suggestive of causation: (1) Thrombocytopenia occurred within a few hours or days after ingestion of the drug. (2) Spontaneous recovery from thrombocytopenia was complete and sustained after the drug was discontinued, this pattern being seen on 2 occasions. (3) Reexposure to acetazolamide resulted in recurrent thrombocytopenia.

However, no specific laboratory test was performed to identify circulating drug-dependent antiplatelet antibodies and to confirm

Figure 1. Timeline of platelet count after first introduction of acetazolamide. Vertical lines indicate period of acetazolamide administration.