no part in the genesis of this lactate, and infusion of A.C.D. bank blood had been stopped previously.

The quantities of lactate and pyruvate circulating during the immediate post-operative period amount to 4 mEq/l. at maximum. No significant change occurs in hydrogen-ion concentrations as a result of these metabolites, and although the reason for their continued production is at present obscure they do not appear to be harmful *per se*.

Summary

Six cases have been studied during reconstructive surgery for aorto-iliac disease. Infrarenal aortic occlusion produces severe desaturation of blood in the lower limb, leading to anaerobic production of lactate. The change in hydrogen-ion concentration produced is small, transient, and not significant at normothermia.

Alterations in hydrogen-ion concentration due to release of anoxic metabolites does not appear to be the cause of systemic hypotension after release of aortic clamps.

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Eczema and Keratoconus

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A series of 100 patients with keratoconus (conical cornea) were examined to test the significance of the occasionally reported association of eczema and this rare eye disease. Eczema has been recorded with keratoconus in 19 patients (François, 1961) since Hilgartner *et al.* (1937) first noted the coincidence. The reported incidence varies widely: all six patients with atopic eczema (Spencer and Fisher, 1959) had keratoconus, and, according to Roth and Kierland (1964), out of 492 with atopic eczema only one had keratoconus. But cataract (Brunsting *et al.*, 1955 ; Rosen, 1959), and perhaps keratoconjunctivitis (Hogan, 1952 ; Thygeson, quoted by Spencer and Fisher, 1959), are accepted accompaniments of atopic eczema.

Investigation

All the patients were attending the Contact Lens Department at Moorfields Eye Hospital, High Holborn. A history was taken. This included details of the following: age at onset of keratoconus, family history, and treatment of keratoconus ; inquiry about types of trauma and habit of eye-rubbing ; right- or left-handed ; past and family history of eczema, asthma, and hay-fever, with age at onset, type, severity, and treatment. Every patient was examined, attention being paid to the following: whole of skin for eczema, particularly of the face and eyelids ; congenital defects of the teeth, hair, finger-nails ; vitiligo, ichthyosis, naevi ; mucous membranes of mouth and conjunctivae ; connective-tissue disorders (Marfan's disease, Ehlers-Danlos syndrome, and cutis laxa).

Findings

Fifty-eight of the patients with keratoconus were males. The age at onset of deterioration of vision which resulted in the diagnosis of keratoconus is shown in the Table ; in 81 patients it was 10 to 25 years. Over half of the series were technicians or professional people, and half appeared to be above average in intelligence ; 85% were Caucasian, 10% Jews, and the remainder Asian or West Indian. There was a family history of keratoconus in six patients.

Age at Onset, Sex, Presence of Eczema in 100 Patients with Keratoconus. Sex Incidence of Eye-rubbers was Approximately Equal

Age at Onset	Males		Females		Eye-rubbers
	Total	With Eczema	Total	With Eczema	
Under 10 ..	4	1	1	—	5
10–20	43	9	22	8	47
21–25	7	1	9	5	8
Over 25 ..	4	3	10	5	11
Total ..	58	14	42	18	71

Eczema.—Thirty-two patients had either signs or a past history of eczema. Fifteen (perhaps 16) of these had *atopic eczema*—among them were three with seborrhoeic distribution of eczema, dandruff, and blepharitis yet with strong past and family histories of atopy. Five had *seborrhoeic eczema* particularly affecting the eyelids. The remainder were more difficult to classify ; three had *lichen simplex chronicus*, with episodes of eye-rubbing, and mild eczema of the eyelids or hay-fever ; two had dyshidrotic eczema or pompholyx (one of whom was probably an atopic) ; three had *contact eczema*, including one patient with nickel allergy and hay-fever. In all patients the eczema preceded the keratoconus ; the interval varied by many years. In six of those with atopic eczema there was a definite history of the eczema spreading to the face and eyelids and being followed in one to two years by the diagnosis of keratoconus. Nine of the eczematous group had hay-fever and six a family history of it. Three of the eczematous patients emphatically denied rubbing their eyes.

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Atopic States in the Non-eczematous Group.—Sixty-eight did not have eczema. Thirty had an atopic background—that is, eczema, asthma, or hay-fever. Eighteen had a history of hay-fever and 18 a family history of atopy, and six had both. Two with hay-fever were on long-term oral corticosteroids. Forty-two of these 68 rubbed their eyes. Five of the six with a family history of keratoconus were in this group.

Connective-tissue and Other Diseases.—Two patients with suspected Marfan's disease, one of them with a suspicious family history, were found to have a normal metacarpal index radiologically and no dislocation of the lenses on slit-lamp examination. A man aged 20 had telangiectatic adenoma sebaceum of the cheeks but did not have epilepsy, mental deficiency, or a positive family history. He had an ichthyotic skin with keratosis pilaris. One patient had knuckle pads, one had a family history of a brother with syndactyly, and another had a brother with a white forelock. One patient who showed extreme sensitivity to sunlight, and her sister with a similar condition, will be further investigated. Three patients had the dominant variety of ichthyosis and one had vitiligo.

Trauma.—Two-thirds of the 100 patients admitted or volunteered that they rubbed their eyes excessively—some told of episodes of uncontrollable intense itching. These urges were initiated by itching in most of the 27 patients with hay-fever and by emotional tension in numerous others, including many of those with eczema. The value of the history of eye-rubbing was not assessed in six patients, and the denial of this practice by four was doubted. Two patients appeared to be proud that they had rubbed through their corneas, puncturing the eyeballs. One was a medical student who said that rubbing his eyes relieved the tension; the other, who had a positive family history of keratoconus, did this at the age of 5. They illustrate the odd mentality of a number of these often intelligent patients. Two patients with keratoconus that has remained unilateral for over five years described strange rubbing habits related to the affected eye—for example, a left-handed man inserted the index finger beneath the left upper eyelid to gouge the sclera with his finger-nail while sucking the dependent thumb.

Discussion

Thirty-two of the 100 patients with keratoconus had some form of eczema. The incidence of eczema in the population is approximately 3% (Service, 1939; Tips, 1954; Readett, 1964); therefore it was 10 times more common in this series than expected. Several of the patients, including the five with seborrhoeic eczema, had some degree of blepharitis. Fourteen cases of keratoconus have been reported in the literature fully enough to diagnose the type of eczema. All were atopics, and it was mentioned that in many the eyelids were affected—these cases include the six found among 1,158 atopics examined in the Mayo Clinic series (Brunsting *et al.*, 1955). A further example was that of a woman aged 28 who had had severe atopic eczema since infancy. She is not included in my series, but her presentation initiated this inquiry. Keratoconus was diagnosed 18 months after the spread of the eczema for the first time to her face and eyelids. In patients whose eyelids were not affected, the flares of eczema could not be correlated with the diagnosis of keratoconus. Half of the 32 eczematous patients had atopic eczema. This is the heritable type that may arise in infancy or childhood, has a characteristic distribution and morphology, and is genetically linked with asthma and hay-fever. Some investigators state that the signs of eczema are mostly the result of trauma (Bobroff, 1962) and that the fundamental disorder is an inherited dysfunction of the small blood-vessels of the skin that may result from a neural (Weber *et al.*, 1955) or humoral (Solomon, 1964) defect.

A personal or family history of atopy is to be expected in about 20% of the population (Carr *et al.*, 1964), but 30 (44%) of the 68 patients without eczema gave a positive personal or family history of atopy or both. Twenty-seven had severe hay-fever, and nine of these had eczema.

Keratoconus is a conical deformity of the cornea which, although it may start on one side only, usually becomes bilateral, is occasionally familial or hereditary (Duke-Elder, 1938; Waardenburg *et al.*, 1961), and has been considered to be an abiotrophy (Mann, 1957). It is rare; there were only 29 (0.15%) cases among 20,000 patients attending an Italian eye clinic (Franceschetti and Caronnes, 1960).

The term "keratoconus" is not specific, as this disease is the end-result of a number of pathological processes. In the present series, cases that followed acute trauma and corneal inflammation have been excluded so far as possible. The remainder comprise a group that could be termed idiopathic, and the aetiology is disputed. Some believe that the basic disorder starts at the anterior cornea, and others that it is in the stroma. Ridley (1962; personal communication, 1964) considers that the disease is initiated by a congenital defect of the posterior cornea.

Anterior Cornea.—The recent electron microscopical studies of Teng (1963), which are supported by Dohlman (1964), suggested that the primary lesion in keratoconus may be a degeneration of the basal cells in the corneal epithelium and that this may liberate proteolytic enzymes, resulting in loss of collagen fibrils and formation of the cone. The liberation of hydrolytic enzymes from lysosomes of connective-tissue cells may be responsible for some of the destructive changes seen in connective-tissues diseases (Weiss and Dingle, 1964).

Stroma of Cornea.—The fibrous tissue in the cornea is collagen (Davson, 1963), but associated with this is mucopolysaccharide ground-substance and a "large quantity of non-collagenous protein, salts, and elastin" (van Walbeek, 1960). At the commonest age for the onset of keratoconus—adolescence—collagen seems to be more susceptible to enzyme and physical degradation (Hall, 1961; Richardson, 1963). That a generalized disorder affecting the stroma of the cornea might be a factor is suggested by the report of keratoconus occurring in one case each of Ehlers-Danlos syndrome (Masci and Scullica, 1962), pseudoxanthoma elasticum (Wollensak, 1961, quoted by Dohlman, 1964), twins with blue sclerotics and elastic-tissue disturbance (Badtke, 1941, quoted by Thomas, 1955), thyrotoxicosis (Delthil and Julou, 1963)—a disease in which regeneration of collagen is impaired (Richardson, 1963)—in 2 out of 47 cases of cutis verticis gyrata (Akesson, 1964), and in Marfan's disease (Storck, 1952, quoted by Waardenburg *et al.*, 1961).

Posterior Cornea.—Cases of idiopathic keratoconus constitute a group with a high incidence of (kerato)conus posticus (Ridley, 1962). This is a rare congenital defect of the central area of the posterior cornea, of which there are two varieties (Stallard, 1930; Butler, 1930).

It is apparent that not all those who rub their eyes develop keratoconus. Yet self-inflicted trauma to the eyeball—excessive eye-rubbing—seemed to be an important factor in the development of keratoconus in two-thirds of the patients, and nearly always preceded the diagnosis of keratoconus. Local irritation of the eyelids due to eczema and hay-fever or emotional disturbances were the usual causes for the eye-rubbing. Their histories recalled the paroxysms of itching experienced characteristically by atopic patients, often in response to minimal stimuli, that precipitate uncontrollable scratching (Sulzberger, 1954). Many non-atopics appeared to behave similarly. One can only speculate on whether prolonged trauma alone can cause keratoconus in any individual. Thus keratoconus seems to be unusually common in mongols (Cullen and Butler, 1963); acute keratoconus, a form undoubtedly associated with trauma, is not unusual, particularly in those with greater mental defect.

The present investigation supports the postulates of Ridley (1962) that trauma to the congenitally thinned and weakened

cornea, (kerato)conus posticus, allows the condition of keratoconus to supervene. The common association of eczema and hay-fever with keratoconus may be explained by the assumption that these diseases provide the stimulus for eye-rubbing.

Summary

Thirty-two patients with eczema, half of whom had the atopic variety, were discovered among 100 patients with keratoconus—10 times the expected number.

Many patients who develop keratoconus have an inherited defect of the posterior cornea—(kerato)conus posticus. Eczema, hay-fever, or emotional disturbance provides the stimulus that causes excessive eye-rubbing, and this may result in conical distortion of the cornea—keratoconus.

Keratoconus should be suspected in young eczematous patients whose vision suddenly deteriorates.

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Some Unusual Cases of Defibrination in Pregnancy

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Defibrination in obstetrics is commonly regarded as being associated with extensive abruptio placentae, amniotic fluid embolism, and intrauterine death of the foetus. The defibrination syndrome, however, may also occur in more unusual cases, and obstetricians should always be on the look-out for this phenomenon. The following three cases, which have occurred in our hospital during the last eight months, serve to illustrate this.

Case 1. Defibrination Associated with Mixed Accidental Haemorrhage. Reversal of Defibrination and Continuation of Pregnancy

A woman aged 23 had a bad obstetric history. She had living children from her first two pregnancies, but the second child required exchange transfusion because of rhesus iso-immunization. Her third pregnancy ended in abortion at 23 weeks: the foetus was hydropic.

In her fourth pregnancy she had a severe mixed accidental haemorrhage at 28 weeks. She required transfusion with 5 pints (2.8 litres) of blood, and was delivered by lower-segment caesarean section. The child weighed 1 lb. 9 oz. (710 g.) and lived only one and a half hours: it was hydropic.

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In her fifth pregnancy she was admitted with severe vaginal bleeding at 26 weeks. The uterus felt rather tense and a diagnosis of revealed accidental haemorrhage was made. The fibrinogen titre was 1 in 2 as compared with the normal 1 in 128 (Sharp *et al.*, 1958). This represents approximately 1/60 of the normal fibrinogen level—that is, 5–10 mg./100 ml. of clottable fibrinogen. Two pints (1.1 litres) of triple-strength plasma and 8 g. of fibrinogen were given as well as 2 pints (1.1 litres) of blood.

Two hours later the fibrinogen titre was normal, and remained so on repeated testing. There was no further bleeding and the pregnancy continued.

The rhesus antibody titre was 1 in 128 anti-D and 1 in 64 anti-C by Coombs on admission. At 33 weeks antibodies to both C and D were present, 1 in 512 by Coombs. (The patient's husband's blood was homozygous rhesus-positive.)

At this time (33 weeks) the foetal heart was noted to be slow and irregular, and lower-segment caesarean section was carried out. A live female child weighing 3 lb. 11 oz. (1,670 g.) was delivered. The placenta was situated in the upper segment of the uterus. There was a mass of solid yellowish blood clot at one edge of the placenta, occupying about one-quarter of the placental surface: the overlying placental tissue was completely infarcted. The placenta weighed 400 g. and the wet weight of the retroplacental clot was 87 g. after lysing as much of the entrapped blood as possible. Bleeding was not troublesome during the operation and the fibrinogen titre was normal.

The baby required repeated exchange transfusions but progressed well. The mother was discharged on her tenth post-operative day.