Wrinkles may be seen in these split-skin preparations, but curiously they show no special features with light microscopy[5] and are probably due to progressive changes with age in the mechanical properties of the dermis.[6] The dermis loses much of its elastic recoil, failing to snap back properly into shape and allowing the skin to hang loosely in folds and wrinkles. Teams of mechanical engineers and biologists studying the way these properties change with age have invented ingenious devices to stretch the skin sideways, in one or more directions, pull it vertically, or deform it with torsional forces or a vacuum. Hammers have even been bounced off it.[7] The problems of interpreting the results of these experiments and of standardising the methods have given rise to a second generation of papers. Perhaps the easiest experiments to follow have been those in which strips of skin were stretched in one direction in vitro, yielding simple stress and strain curves. The initial deformation seems to be controlled by the network of fine elastic fibres in the dermis, and the elastic recovery of these is reduced in old age—or they may be digested away enzymatically.[6] As stretching continues an increasing number of collagen fibres are straightened and take up some of the load. Finally, when all collagen fibres are straight, little further stretching is possible. This loss of elasticity of old skin must be related to those changes in the elastic fibres which can be seen with the electron microscope to consist of a decrease in microfibrils, an increase in electron-dense inclusions, and the appearance of vesicular structures.[8]

If living skin is compressed rather than stretched another set of age-related changes may be observed. No differences between young and old skin appear during the loading phase; but after the pressure has been removed young skin quickly returns to its normal thickness while in an old person full recovery may take as long as 24 hours.[6] This effect is thought to be due to changes in the dermal ground substance.

In old age the dermis also becomes thinner. The simple measurement of histological preparations is fraught with difficulties,[9] and newer techniques have been devised including high-frequency pulsed ultrasound,[10] specialised radiography,[11] and the use of callipers.[9] Thinning occurs progressively during adult life in men but seems to start only after the fifth decade in women.[12] Skin collagen falls by about 1% a year throughout adult life, and since it decreases more quickly than skin thickness the density with which collagen is packed into the dermis also decreases. Collagen itself seems to become more stable with advancing age, but the possible increase in cross-linkage between adjacent molecules which was suggested by thermal shrinkage studies[13] has yet to be confirmed. With age fewer fibroblasts are seen in the dermis, many showing ultrastructural changes which are suggestive of reduced biosynthesis,[14] and wound healing also slows. Most dehiscences of abdominal incisions occur in elderly patients—though complications of this kind still affect only a minority of even very elderly patients having surgery.

Indeed, the main trouble with old skin is the way it looks rather than the way it behaves, and here exposure to the sun is a major factor. The bronzed young skins of today will become the wrinkled prune-like ones of tomorrow. Sadly the words of Thomas Nashe are more appropriate now than when he wrote them 400 years ago:

"Beauty is but a flower
Which wrinkles will devour."

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Diagnosis and treatment of lactose intolerance

In most mammalian infants, including man, the disaccharidase enzyme lactase is found in the brush border of the villus epithelial cells of the small intestine. In animals the tissue lactase activity drops sharply at the time of weaning. The human species is unusual in that in some (but not all) racial types intestinal lactase persists into adult life—probably as a result of selective pressures which allowed persistence of a mutant gene in these ethnic groups. Races whose ancestors were Northern Europeans, African pastoralists, or residents of the north-west part of the Indian subcontinent have a high probability of being lactose digesters in adult life, whereas most Negroes, Asians, and South Americans are lactose malabsorbers.[1 2] Population movements in the past 100 years have now combined with expansion of the dairy industry beyond the temperate zones with the result that many lactase-deficient adults now live in societies where foods containing lactose, principally in cows' milk, are important and regular dietary constituents.

Malabsorption of lactose does not always lead to lactose intolerance. The adverse reactions which may develop after ingestion by a lactase-deficient individual of foods containing lactose include nausea, bloating, abdominal pain, and diarrhoea.[3 4] When these symptoms occur after ingestion of cows' milk, however, they are not necessarily due to lactase deficiency: allergic reactions to food may have similar clinical effects.[5 6] The clinical effects of lactose ingestion are, indeed, related to dose with a wide variation among individuals. The conventional lactose load used in tolerance tests, 50 g, will produce symptoms in 70-80% of malabsorbers, whereas 10-15 g lactose, or half a pint of milk, will produce abdominal symptoms in only 30-60%.[7-9] Intolerance to lactose has nutritional implications. Whereas most of those affected consider the condition merely an inconvenience, inevitably they drink less milk than do those who are lactose tolerant.[8 10] Skimmed milk supplied to Third World countries as a protein

supplement may be rejected by both adults and children because it causes diarrhoea.[4]

There are no data on the prevalence of lactose malabsorption and intolerance, and the age distribution of persons concerned, in different racial groups in Britain. Clinical practice suggests, however, that lactose malabsorption occurs in up to 80% of non-white adults but in fewer than 5% of white Britons. Thus most, but not all, patients in whom lactose intolerance is diagnosed will be immigrants to Britain and their descendants. Lactose intolerance should be the primary diagnosis in a number of patients with "idiopathic" diarrhoea, the irritable bowel syndrome, recurrent abdominal pain, and post-gastrectomy symptoms. A coincident lactose intolerance may modify the pattern of clinical presentation of gastrointestinal or other diseases, and a period on a lactose-free diet may often be of diagnostic value in patients with abdominal pain or malabsorption.

Since the clinical effects of lactose intolerance are produced by altered gastrointestinal motility, some patients' symptoms will suggest the diagnosis of the irritable bowel syndrome. In a study conducted in Oxford, lactase deficiency was documented in nine of 73 patients with the irritable bowel syndrome who were British natives and seven of eight patients with the irritable bowel syndrome who were non-British.[11] Nevertheless, symptoms were relieved by a lactose-free diet in only six of the 16 patients with the irritable bowel syndrome with lactase deficiency; all the others required supplementary treatment directed at the bowel motility disorder. The racial predilection to lactose intolerance in patients with the irritable bowel syndrome was confirmed in a study of doctors with these syndromes,[10] and some patients with both disorders are highly sensitive to lactose.[12 13] Even though lactose intolerance is a factor in only a few of the patients who present to the gastroenterologist with irritable bowel syndrome, the possibility should be considered in any non-white patient with the syndrome and also in those with watery diarrhoea or greatly excessive production of flatus.

Recurrent abdominal pain in children is almost as common as irritable bowel syndrome. The "postweaning" drop in intestinal lactase activity may occur as early as 5 years of age, so that schoolchildren may be intolerant to lactose. A prospective study of recurrent abdominal pain in children in the United States showed malabsorption of lactose in 16 of 59 white children and 16 of 21 non-whites, with 70% of lactose malabsorbers also having clinical lactose intolerance.[14] No similar study of non-white children seems to have been published in Britain, but investigation of 26 white children in Leeds who presented with recurrent abdominal pain found malabsorption of lactose only in three, of whom two developed abdominal pain after taking lactose.[15]

Gastric surgery radically alters the physiology of the upper gastrointestinal tract. Lactase-deficient individuals in whom milk caused no ill effects before surgery may develop bloating, dumping, and diarrhoea after partial gastrectomy or other operations on the stomach and duodenum.[16 17] These patients often recognise that milk, even in small amounts, precipitates or exacerbates their symptoms.

As with other states of food intolerance, the strict diagnosis of lactose intolerance relies on objective measurements of the clinical effects of the withdrawal and reintroduction of lactose. Milk is, however, such an important nutrient that in each patient milk intolerance should be confirmed as being due to lactase deficiency by some other technique. The presence of lactose malabsorption can be diagnosed by lactose-tolerance tests,[18] by detection of hydrogen in the breath after a lactose load,[19] or by assay of lactase in a jejunal biopsy specimen.[3 4] Virtually all lactose malabsorbers have diarrhoea, borborygmi, abdominal pain, and bloating after ingestion of 50 g lactose.

The only satisfactory treatment of lactose intolerance is a low lactose diet—lactase is not an adaptable enzyme.[20] Older children and adults should be reassured that the symptoms of lactose intolerance are not due to any disease and can readily be prevented by manipulation of diet. Foodstuffs high in lactose, such as fresh milk, powdered milk, and milk puddings, should be avoided, but most patients can tolerate fermented milk products and the small amounts of milk used in baking and added to margarines and sausages. If the patient's symptoms are entirely due to lactose intolerance response to this treatment will be excellent. As emphasised, however, lactose intolerance often coexists with other disorders such as abnormal intestinal motility, and these must be treated independently by dietary or other means.

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