11 Sid and Cad

The Sid antigen Sd\(a\) (ISBT Nr. 901 012) is inherited as a dominant autosomal character [38,55]. It is not confined to red cell membranes but occurs also in different tissues and body secretions. In about 96% of humans this specificity is present on erythrocytes and/or in secretions as well; 4% lack Sd\(a\) activity and contain strong anti-Sd\(a\) in their serum [44].

There is considerable variation in the strength of Sd\(a\) antigen in different individuals [38,55]: only 1% of the red cell samples are strongly agglutinated by anti-Sd\(a\) antibodies, 80% show a moderate reaction with partial agglutination; in approximately 20% of the Sd(a+) individuals the Sd\(a\) antigen is scarcely detectable on the erythrocytes, and the Sid phenotype can be determined only by testing body secretions for Sd\(a\) substance.

Studies of tissues and secretions [44,45] show that high Sd\(a\) activity can be found in kidneys, stomach, and colon, whereas this specificity is only weakly expressed or totally absent in other tissues. The main sources of water-soluble Sd\(a\) active material are urine and meconium; saliva and gastric juice show only low Sd\(a\) activity.

The occurrence of Sd\(a\) in the human organism is age-dependent. The antigen cannot be detected on the erythrocytes of infants under ten weeks [38]. In foetuses Sd\(a\) is equally distributed along all segments of the intestinal tract, in adults, however, it is found only in gastric and colonic mucosa [51]. Saliva of newborn infants contains about four times the Sd\(a\) activity present in the saliva of adults [44].

In pregnancy the Sd\(a\) activity of erythrocytes is significantly reduced — about 75% of all pregnant women are Sd(a–), whereas the Sd\(a\) activity of urine is not influenced [51].

Further, the expression of Sd\(a\) antigen dramatically decreases in malignantly transformed cells [21,53].

Sd\(a\) active material is not confined to humans but is found widely distributed in tissues and body fluids of various species of mammals; the urine of guinea pigs in particular has proved an excellent source of water-soluble Sd\(a\) substance [44]. In birds Sd\(a\) antigen has not been detected to date.

Cad [14,37] is a rare human red cell antigen which is also inherited as an autosomal dominant character [75]. It is characterised by its strong reactivity with the
N-acetylgalactosamine-specific lectin of *Dolichos biflorus*. Since *Cad* erythrocytes are agglutinated by the majority of normal human sera this serological property is often considered a form of polyagglutinability. Further investigations show, however, that this phenomenon is caused by the weak anti-\(Sd^a\) antibodies frequently found in human sera [54]. Sanger et al. [57] have already proposed that *Cad* may be a very intense form of \(Sd^a\) (\(\rightarrow Sd(a++)\) or 'Super-Sid', see also [54]). Indeed, structural and biochemical investigations on \(Sd^a\) and *Cad* determinants confirm a close similarity between these antigens (see below), although their distinct serological differences cannot yet be explained.

It should also be mentioned here that during *in vitro* experiments a remarkable resistance of *Cad* erythrocytes towards infection by the malaria parasite *Plasmodium falciparum* was noted [13].

Two examples of a cold agglutinin unrelated to the I, Pr, and Gd blood groups were described by Marsh et al. [42]. As the antibodies were inhibited by urine from \(Sd(a+)\) persons, a relationship to the \(Sd^a\) blood group was assumed and the autoantibodies were named anti-\(Sd^x\). Subsequent investigations by Bass et al. [2], however, showed that the inhibition was a nonspecific effect caused by charged molecules, and no direct association with the Sid blood group could be found. The authors therefore recommend that the antibody be renamed anti-Rx (after the initials of the original proposita).

### 11.1 Antisera and Lectins

Anti-\(Sd^a\) is a relatively common antibody found in small quantities in nearly all human sera [54]; it reacts preferentially with \(Sd(a++)\) (= *Cad*) erythrocytes. The only useful form of anti-\(Sd^a\) is found in the sera of \(Sd(a-)\) individuals [55].

Two hybridoma antibodies directed towards murine cytotoxic T cells have turned out to be anti-\(Sd^a/Cad\) specific [16]. More recently two *Cad*-specific hybridoma antibodies (2A3D3 and 2D11E2) have been produced using gangliosides from human hepatocellular carcinoma cells as immunogens [34].

Specific, naturally occurring anti-*Cad* has been detected in chicken serum [7]; it can also be produced by immunisation of the animals with *Cad* erythrocytes. Anti-*Cad* specific lectins occur in *Dolichos biflorus* [3,57], *Vicia villosa* [71], *Salvia hormium* and *Salvia farinacea* [4,6]. Extracts from *Salvia* seeds also contain an anti-*Tn* agglutinin (see Sect. 10.6), which in most cases can be removed by absorption with *Tn* erythrocytes; the anti-\(A_1\) specificity of the *Dolichos biflorus* lectin (see Sect. 5.2.1), however, cannot be separated from its anti-*Cad* specificity [54].