The building that today houses most of the collections of the Museo de Santa Cruz is an excellent example of transitional Gothic-Renaissance civil architecture in Spain. We can say that the relationship between the content and the container is more than interesting in this museum. Cardinal Pedro González de Mendoza, Archbishop of Toledo since 1482, in the style of the Italian patrons of the time, ordered its construction as a hospital for orphaned minors and the homeless. For this, in 1494 he received a bull from Pope Alexander VI, and decided to do it in honor of the Holy Cross of Jerusalem, of which he was very devoted.

Died in 1495, therefore unable to see his project even started, in his will he donated enough resources to be able to found a hospital in Toledo "to welcome and cure the sick, and to raise foundlings". His testamentary executors were Queen Isabel the Catholicf, Cardinal Cisneros and his nephew, the Archbishop of Seville Diego Hurtado de Mendoza. They took it upon themselves to fulfill his will.
During the second half of the 15th century, Toledo was a very rich city thanks to the goldsmith, silk and weapons industries (its steel has been famous since Antiquity). On the other hand, ceramics in general and tiles from the Muslim tradition in particular have an important presence in the city. To this must be added the fact that Toledo is the primary headquarters of the archbishopric of Spain, and throughout the Late Middle Ages and the Modern Age it is also a major center of political power.

The hospital was built in this context, and the fact that Toledo was such an important city at the time also affected its location, in an area far from the religious/political center of the city and with a steep slope, which will be a first challenge for its architects. The reality is that there was no enclosure large enough to house the hospital in a more central area of the city.
On the other hand, in Castilla, unlike in Aragon, there are hardly any examples of civil Gothic architecture. This transfers to the master builder, Enrique Egas, an added problem, because when Mendoza, or the Catholic Monarchs, began to commission hospitals, there will be no model for this type of building in Castilla and its area. Therefore, Egas decided to adopt a "modern" plan for the hospital, because he finds it functional and practical. He chose stone walls, but wooden coffered ceilings, easier to make than ribbed vaults, which would also have given the complex an ecclesiastical character that was to be avoided in this case.

However, if we talk about hospitals at that time, they are for "curing" both the body and the soul, and they would be inconceivable otherwise. Hence the placement of a high altar in the transept, under the lantern, also very functional because religious services could be followed from anywhere in the building.
The architects, the brothers Antón (tracer) and Enrique (director of the work) Egas conceived a layout inspired by the cruciform structure of the Ospedale Maggiore in Milan (work of the Italian architect Antonio Filarete). We can find other Egas buildings with a similar plan: the Hospital of Santiago de Compostela and the Hospital Real de Granada. The original idea would be an Italianate plan with Gothic decoration.

It is a new typology, since it will not be a charity hospital attached to a convent or a church as was traditionally the case. It is inspired by Italian models and in turn will serve as a model for other buildings, such as the El Escorial monastery itself.

The project consists of a plan formed by a large Greek cross inscribed in a square, giving rise to four cloisters. Finally, only two courtyards were executed, and later a smaller third one.
In the transept there is a dome of the Caliphate tradition topped by a high dome. In this way, the interior space is grandiose, because the upper floor opens onto the transept and is not covered.

An altarpiece was placed at the head of the north nave, today in the church of San Juan de los Reyes.

There are coffered ceilings, from Toledo Mudejar tradition on the upper floor, and with Renaissance caissons on the lower floor. The upper floor would be used for children and the lower floor for the rest of the hospital users. It is worth noting the delicate ornamentation on the transept pillars, with a mixture of Gothic, Mudejar and Renaissance elements.
2nd constructive stage: around 1530

Alonso de Covarrubias carried out the second phase of the construction of the hospital. He is in charge of the courtyard or noble cloister, the staircase and the vestibule, and to whom the doorway is attributed.

The cloister is a good example of the first Spanish Renaissance from the beginning of the 16th century, already in full classicism in Italy but still in its infancy in the Iberian Peninsula. The Renaissance arches on the ground floor, all with Jerusalem cross medallions on the spandrels, provide balance, creating an open and harmonious space, where perfection of detail is more important than ornamental accumulation. The typical elements of the Florentine Quattrocento are used, but with another disposition. The upper floor is still reminiscent of Gothic, with lowered arches and a lattice that closes the perimeter of the courtyard, and in which Mendoza family coats of arms appear as a decorative motif.
The monumental staircase of the Museum of Santa Cruz is considered to be the most beautiful of the Spanish Plateresque still standing. In order to design it, Covarrubias was forced to follow the lines previously marked out by Egas. It consists of three arches in the front, two of them lowered (the sides) and a central round one. It is decorated with isolated flowers and crosses in the free spaces. The three arches are supported by two columns with a smooth shaft and a composite capital, of fine carving, and on two lateral pilasters with Plateresque shafts with grotesques. The decorative set is completed with coats of arms of the Mendozas and horns of plenty, in a clear propaganda effort.
The stairwell is preceded by a barrel vault with caissons and rosettes, and includes padded walls in the style of the first Florentine Renaissance, repeating the decorative themes of the Jerusalem cross and the Mendoza coat of arms. As in other Renaissance stairs, despite the small space, the staircase, made up of three sections, is monumental.

The railing begins with a column with a reticulated shaft with a rosette, a big flower and the cardinal's coat of arms. The balusters, with entasis in the center and finely carved, will be widely reproduced in later buildings. Another triple arcade, similar to the first, leads to the upper gallery. The complex is covered with a coffered ceiling, with Renaissance caissons in the center and fans in the corners.
As for the façade of the building, in principle it corresponds to a typically Spanish façade, with a bare wall and decoration concentrated on the cover. This presents a lintelled opening and a semicircular tympanum, with figures of Cardinal Mendoza (worshipping the Holy Cross) and Saint Helena, Saint Peter and Saint Paul, and two smaller figures at the ends. According to Christian tradition, Saint Helena, wife of Emperor Constantius Chlorus and mother of Emperor Constantine I, converted to Christianity after being abandoned by her husband. Tradition also relates her to the search for the relics of the True Cross, which she would have finally found. Hence her presence on the front of the hospital, built under the invocation of the Holy Cross of Jerusalem at the express wish of the Cardinal.
Perhaps as a reflection of the transition from Gothic to Renaissance, surrounding the tympanum there are a series of archivolts, decorated with crosses and angels under canopies and grotesques, which carry on a pair of columns on each side of the door, with their corresponding pedestals.

In the upper part of the archivolts, occupying a central position, we see a female image that represents charity, surrounded by children, and that recalls the purpose of the building. The four female figures in the intercolumns are identified with the four cardinal virtues.

In the second body of the portal there is a central niche that reproduces the embrace of Saint Anne and Saint Joaquin in front of the Golden Gate of Jerusalem, while in the side niches there are figures of patriarchs. Next to them are two windows with Plateresque frames. Above the general line of the eaves, a last body stands out, with five balustraded columns and four lintelled openings topped by a pediment, once again with the coat of arms of the Mendoza family supported by angels as the main decorative motif, which we also see repeated on the lintel of the main doorway opening.