A MILD DEGREE of pulmonary arterial hypertension associated with an increased pulmonary vascular resistance is a normal feature in people living at high altitudes. It has been recently demonstrated that a considerable number of muscularized pulmonary arterioles is present in these people at all ages. This fact gives indeed an anatomic substratum to the hemodynamic findings. The well-known occurrence of right ventricular hypertrophy in adults and children living at high altitudes can now be better understood.

In the present paper, the evolution of the elastic configuration of the pulmonary trunk in people native to high altitudes is described.

Heath, Wood, DuShane, and Edwards have pointed out that in cases of cardiac septal defects associated with pulmonary hypertension from birth, the "aortic" type of pulmonary trunk could be maintained to the third and fourth decades. When pulmonary hypertension was secondary to an acquired cardiac disease, as in mitral stenosis, the already established "adult" type of pulmonary trunk did not change. Cases of pulmonary stenosis with pulmonary arterial hypertrophy exhibited a pulmonary trunk media almost completely devoid of elastic tissue.

The evolution of the elastic configuration of the pulmonary trunk at high altitudes strongly suggests that pulmonary hypertension is the determining cause of the differences found in relation to sea level cases.

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Material and Method

Five hundred and fifty cases were studied. Two hundred and sixty-seven correspond to natives of communities located between 11,300 to 14,900 feet above sea level, in the central Andean region of Perú. Two hundred and eighty-three cases from Lima (500 feet above sea level) were used for comparison. They were selected at random from material subjected to a previous study.

The ages varied from birth to 78 years in high altitude cases and from birth to 80 years in cases at sea level. In the two groups, both sexes were represented approximately in the same proportions.

Cases with prolonged residency in places with appreciable differences in altitude from that of origin were excluded.

Accidents were responsible for most of the adult deaths in high altitude. Acute bronchopneumonia caused more than 90 per cent of deaths in the first 3 years of life. No cases with cardiac malformation or cardiovascular disease are considered in the present study.

The autopsies of high altitude cases were performed mainly at Cerro de Pasco (altitude, 14,300 feet) and La Oroya (altitude, 12,375 feet). Tissue samples of pulmonary trunk and ascending aorta were obtained and prepared for histologic examination in the same manner as previously indicated.

A "blind" study of the elastic configuration of the pulmonary trunk and ascending aorta was carried out. In every case, the pulmonary trunk was classified according to one of the following types: "aortic," "persistent," "transitional," and "adult." A description of the characteristics of these elastic configurations has been given elsewhere. For the sake of simplicity no distinction was made between "transitional-A" and "transitional-B" models.

Two observers working separately made five readings of the whole set of sections. For a given case a correct reading was accepted to be that repeated four or five times. The number of readings was at least 2,750 per observer, and 5,500 in total for both observers. The cases read differently by the observers—less than 6 per cent of the total—were classified after a discussion of their characteristics.
**Results**

The results are presented in relation to three different altitude levels. The altitude of Lima, where control cases came from, was considered level I (birth to 3 months, 39 cases; 4 months to 9 years, 90 cases; 10 to 30 years, 64 cases; over 30 years, 90 cases). Level II comprised 152 cases with birthplaces and residences between 11,300 to 12,600 feet above sea level (birth to 3 months, 25 cases; 4 months to 9 years, 38 cases; 10 to 30 years, 45 cases; over 30 years, 44 cases). One hundred and fifteen cases of those born and who lived permanently in places situated between 13,250 to 14,900 feet of altitude were grouped in level III (birth to 3 months, 29 cases; 4 months to 9 years, 25 cases; 10 to 30 years, 25 cases; over 30 years, 36 cases) (fig. 1).

**“Aortic” Type of Pulmonary Trunk**

This elastic configuration was present from birth to 2 months and 23 days in level I, from birth to 3 years in level II (figs. 2A and 2B), and from birth to 9 years in level III (figs. 3A, 3B, and 3C).

In the age range of presentation the “aortic” configuration accounted for 64 per cent of cases in level I, for 64 per cent in level II, and for 85 per cent in level III.

**“Persistent” Type of Pulmonary Trunk**

The “persistent” type was present from 1 month to 5 years in level I, from 10 months to 54 years in level II (figs. 4A and 4B), and from 1 to 72 years in level III (figs. 4C and 4D).

In the age range of presentation, the “persistent” configuration accounted for 16 per cent of the cases in level I, for 60 per cent of those in level II, and for 75 per cent in level III.

This was the only type of elastic configuration observed in the 4- to 14-year cases in
level II and in the 10- to 47-year cases in level III.

"Transitional" Type of Pulmonary Trunk
Cases with the "transitional" configuration were found from 25 days to 6 years in level I and from 3 to 18 months in level II (fig. 2C). No cases with this configuration were found in level III.

In the age range of presentation, the "transitional" configuration accounted for 55 per cent of the cases in level I. Nine of 19 cases between 3 to 18 months in level II exhibited the "transitional" configuration.

"Adult" Type of Pulmonary Trunk
Cases with the "adult" type were observed from 12 months to 80 years in level I (fig. 5B), from 15 to 72 years in level II, and from 48 to 78 years in level III (fig. 5A).

This elastic type constituted the totality of cases over 6 years in level I and over 54 years in level II. In level III, 3 of 4 cases over 60 years exhibited the "adult" type of pulmonary trunk.

Discussion
In people born and living permanently at high altitudes, the evolution of the elastic configuration of the pulmonary trunk differs notably from that observed at sea level. An abnormal maintenance of the "aortic" type of pulmonary trunk and a great incidence of the "persistent" configuration, even in adult life, are the main features in high altitude dwellers compared with those at sea level.

The separation of high altitude cases into two groups, according to the altitude of their place of birth and permanent residence, has led to the recognition of two distinct pathways in the evolution of the elastic configuration of this artery. They will be briefly summarized.

Evolution of the elastic configuration of the pulmonary trunk in level II (11,300 to 12,600 feet above sea level). Although the "aortic" configuration was observed in the first 3 years of life, some cases showed structural evolutionary changes at an earlier period. The "transitional" and "persistent" types were noticed in the course of the first 12 months of life. In variance with what occurred in level I (sea level), "transitional" configura-

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**Figure 2**
A, upper left. J.C., a 3-year-old boy from La Oroya (altitude 13,375 feet). Pulmonary trunk of "aortic" type, × 160. B, upper right. S.F., a 13-month-old daughter of white North Americans living at La Oroya. Pulmonary trunk of "aortic" type. At sea level this elastic configuration is normally observed only up to the third month. Despite racial differences, the pulmonary trunk of this child behaved like those of Peruvian natives at high altitude. × 160. C, lower. T.S., a 4-month-old boy from La Oroya. Pulmonary trunk of "transitional-B" model. × 160. All photomicrographs stained with Weigert's fuchsirn-resorcin for elastic tissue, counterstained with Van Gieson's picro-fuchsirn.
STRUCTURE OF THE PULMONARY TRUNK


Evolution of the elastic configuration of the pulmonary trunk in level III (13,250 to 14,900 feet above sea level). Here, the "aortic" configuration accounted for most of the cases in the first 9 years of life. Since the "transitional" configuration does not occur at this level, it seems quite clear that the "aortic" type evolves exclusively and directly in the "persistent" type. Conversion of the "persistent" to the "adult" configuration takes place very late in life.

Right heart catheterization studies performed at high altitudes by Rotta, Caneza, Hurtado, Velásquez, and Chávez,1 Peñaloza, Sime, Banchero, Gamboa, Cruz, and Marticorena,2 Sime, Banchero, Peñaloza, Gamboa, Cruz, and Marticorena,3 Vogel, Weaver, Rose, Raymond, Blount, and Grover,4 have provided necessary information for understanding most of the features of the present report.

Sime et al.,3 at Cerro de Pasco (14,300 feet), found an average mean pulmonary pressure of 45 ± 6.7 mm Hg in children from 1 to 5 years; and 28 ± 2.0 in children from 6 to 14 years. These values are definitely higher than those accepted as normal in comparable ages at sea level.11

The presence of the "aortic" type of pulmonary trunk up to the first decade, as observed in level III, agrees with the existence of pulmonary hypertension as reported by Sime et al.3 No hemodynamic studies have been performed in children in altitudes corresponding to level II. The finding of right ventricular hypertrophy in these children8 is indeed an indication of the existence of pulmonary hypertension. Therefore, the occur-

Circulation, Volume XXVII, June 1963
G.C., a 48-year-old man from Cerro de Pasco. This pulmonary trunk was classified as "adult." However, a greater content of elastic fibers than that observed in "adult" cases from sea level can be seen (compare with B). There exists in addition an increase in the elastic filamentous component, a characteristic also observed normally at sea level in cases of this age. × 160.

S.T., a 40-year-old man from Lima at sea level. Pulmonary trunk of "adult" type. × 160.

P.T., an 11-year-old girl from La Oroya. Pulmonary trunk of "persistent" type, highly rich elastic media in which long fibers alternate with fragmented ones. × 160.

T.L., a 28-year-old man from La Oroya. Pulmonary trunk of "persistent" type. × 160.

J.N., a 14-year-old boy from Carhuamayo (altitude 13,500 feet). Pulmonary trunk of "persistent" type. × 160.

R.S., a 36-year-old man from Cerro de Pasco. Pulmonary trunk of "persistent" type. × 180.

The maintenance of the "aortic" configuration of the pulmonary trunk at high altitudes brings to mind what occurs in congenital cardiopathies associated with pulmonary hypertension from birth. This characteristic can be interpreted as evidence that high altitude pulmonary hypertension begins very early in life, probably from birth.
Rotta et al.,4 in Morrococha (14,900 feet), found in four healthy natives, age 20 to 34 years, an average mean pulmonary pressure of 24 mm. Hg, a value double that obtained in a control group at sea level. More recently, Peñaloza et al.2 carried out right heart catheterization studies in 38 young adults born in places between 12,000 to 14,900 feet above sea level. Those authors reported an average mean pulmonary pressure of 28 ± 1.7 mm. Hg, in comparison to 12 ± 0.4 mm. Hg found in a sea level control group. Vogel et al.,4 in Leadville (10,150 feet), have found in a group of children between 13 to 17 years, an average mean pulmonary pressure of 25 mm. Hg.

The presence of the "persistent" configuration of pulmonary trunk, as observed in high altitude dwellers, can certainly be ascribed to the reported occurrence of a mild degree of pulmonary arterial hypertension in these people.

It has been recently pointed out that, in human beings, a relationship exists between the magnitude of pulmonary arterial pressure and the altitude level of residency: higher pulmonary pressure figures at higher altitudes.4 This would certainly explain why in level III the "aortic" type of pulmonary trunk is three times greater in the age range of presentation than in level II. The greater incidence of the "persistent" configuration and its longer age range of presentation in level III, when compared with level II, could also be explained on the same basis.

The absence of "transitional" cases in level III suggests that a significant postnatal fall of pulmonary arterial pressure, as is the case normally at sea level,11 does not occur at this altitude. It seems that a gradual diminution of pulmonary pressure, determining a minor degree of anatomic change, takes place. Thus, the "aortic" type evolves smoothly into the "persistent" type.

Contrarily, a postnatal fall of pulmonary pressure of some significance can be suspected in level II, by the finding of cases with the "transitional" configuration. It is of interest that in a re-study all these "transitional" cases have been found to correspond to what has been designated the "transitional-B" model, i.e., they exhibited a majority of fibers partially disintegrated but not fragmented16 (fig. 2C). It may be that, in level II, a mild degree of pulmonary hypertension acting on fibers that have not lost their continuity can stimulate the regeneration of many long fibers, thus determining the establishment of the "persistent" configuration. This possibility would explain why, even when the "transitional" configuration is present, there is an appreciable delay in the appearance of the "adult" type.

Finally, the finding of the "adult" type of pulmonary trunk at high altitudes suggests that, even in the higher altitude level, pulmonary hypertension subsides progressively with age.

**Summary and Conclusions**

In a "blind" study two observers determined the type of elastic configuration of the pulmonary trunk in 267 high altitude dwellers, of all ages, who died accidentally or due to noncardiovascular diseases. A sea level group of 283 cases, of comparable ages, served as control.

It has been shown that in places between 13,250 to 14,900 feet above sea level, the evolution of the elastic configuration of the pulmonary trunk is characterized by the maintenance of the "aortic" type up to 9 years. This elastic type evolves exclusively into the "persistent" configuration, which is observed for the rest of life. However, conversion of the "persistent" type into the "adult" type can be observed, especially after 60 years of age.

In places located between 11,300 to 12,600 feet of altitude, the "aortic" type of pulmonary trunk is retained up to 3 years. Cases with the "transitional" configuration can be observed, but apparently they rapidly evolve into the "persistent" type. This elastic configuration is observed principally in childhood and adolescence and is also present in a great proportion of young adults. By 35 years, ap-
proximately, the totality of cases has become of "adult" type.

The above described pathways of evolution of the elastic configuration of the pulmonary trunk differ notably from what is normally observed at sea level. They are determined, without doubt, by the existence, at high altitudes, of a mild degree of pulmonary hypertension from birth. Differences between the two high altitude groups studied should be related to the occurrence of higher pulmonary pressure values at higher altitude levels.

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Studies on the Structure of the Pulmonary Trunk: II. The Evolution of the Elastic Configuration of the Pulmonary Trunk in People Native to High Altitudes
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