The Effect of Valvular Heart Disease on Maternal and Fetal Outcome of Pregnancy
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OBJECTIVES
The aim of this study was to evaluate the association between valvular heart disease (VHD) and maternal and fetal outcome in a relatively large group of patients by a comparison to a well-matched control group.

BACKGROUND
Available information regarding outcome of pregnancy in women with VHD is limited to either anecdotal reports or small series of patients without an appropriate control. A better understanding of the effects of valvular abnormalities on pregnancy outcome is of value for risk assessment and the design of a therapeutic plan.

METHODS
A retrospective evaluation was made of 66 pregnancies in 64 women with VHD cared for at a tertiary-care center with a high-risk obstetrics/cardiology clinic and 66 individually selected normal pregnant women matched in age, ethnicity, obstetrical and medical history, time of initial prenatal care, and year of pregnancy.

RESULTS
Women with VHD had a significantly higher incidence of congestive heart failure (38% vs. 0%; p < 0.00001), arrhythmias (15% vs. 0%, p = 0.002), initiation or increase of cardiac medications (41% vs. 2%, p < 0.00001), and hospitalizations (35% vs. 2%, p < 0.00001). Mortality, however, occurred in only one patient (2% vs. 0%, p = NS) with aortic stenosis (AS) and coarctation. Moreover, VHD also had an effect on fetal outcome, resulting in an increased preterm delivery (23% vs. 6%, p = 0.03), intrauterine growth retardation (21% vs. 0%, p < 0.0001), and a reduced birth weight (2897 ± 838 g vs. 3366 ± 515 g, p = 0.0003). Increased maternal morbidity and unfavorable fetal outcome were seen mostly in patients with moderate and severe mitral stenosis (MS) and AS.

CONCLUSIONS
Pregnancy in women with MS and AS is associated with marked increase in maternal morbidity and unfavorable effect on fetal outcome, which are related to severity of disease. Despite high maternal morbidity, mortality is rare. (J Am Coll Cardiol 2001;37:893–9)

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Management of pregnancy in patients with valvular heart disease (VHD) continues to pose a challenge to the clinician. Although the risks in such patients have been recognized (1), they have not been well defined because available information is based mostly on anecdotal reports or small series of patients without an appropriate control population (2–4).

The present study was, therefore, designed to evaluate the effect on VHD on maternal and fetal outcome in a relatively large group of patients cared for in a single institution by a comparison with a well-matched group of normal pregnant women.

METHODS
The study was designed as a retrospective evaluation of pregnancy outcome in patients with VHD in comparison to that of normal controls. All cases were followed during pregnancy, labor, and delivery at the Los Angeles County/University of Southern California Medical Center, a tertiary-care facility with a high-risk obstetrics/cardiology clinic, and the study protocol was approved by the institutional review board of the LAC/USC Medical Center. Exclusions included: 1) incomplete records, 2) prosthetic heart valves, and 3) therapeutic abortion for noncardiac reasons. The study population was divided into three major subgroups based on their predominant valvular disease (i.e., mitral, aortic, and pulmonic valve). Mitral stenosis (MS) and aortic stenosis (AS) were classified according to calculated valve area established by either cardiac catheterization or echocardiography as mild for valve area >1.5 cm², moderate 1.0 to 1.5 cm², and severe <1.0 cm² (5). Four patients with predominant mitral regurgitation (MR) were included in the mild group. For each studied patient, a control case was selected individually from delivery records at the same Medical Center to match the patient in age, ethnicity, obstetrical and medical history, time of initial prenatal care, and year of pregnancy. Separate control cases were used to match two different pregnancies in two of the patients.

Data analysis. The data were analyzed to evaluate maternal as well as fetal outcome. Criteria for maternal outcome included: 1) change in New York Heart Association (NYHA) functional class; 2) new onset of congestive heart failure (CHF); 3) hospitalizations not related to labor and...
delivery; 4) new onset or exacerbation of arrhythmias; 5) need either to initiate or enhance dose of cardiac medications; and 6) mode of delivery. Criteria for fetal outcome included: 1) preterm labor, 2) stillbirth, and 3) birth weight.

Comparisons of baseline characteristics and the criteria evaluated for maternal and fetal outcome between patients with valvular disease and controls were performed using the two-tailed Fisher exact test. Patients’ ages, duration of pregnancy and neonatal birth weights were compared with the use of a nonpaired t test. All values were presented as mean ± SD. Statistical significance was accepted at the 95% confidence level (p < 0.05).

RESULTS

Patient population. Sixty-six pregnancies in 64 patients met the inclusion criteria and were included in this study. There were 46 pregnancies in 44 patients with predominant mitral valve disease. Nineteen of these pregnancies occurred in patients with mild, 18 in moderate and 9 with severe MS. Additional valvular abnormalities included MR in 12 patients, MR and mild AS in 1 patient, aortic regurgitation (AR) in 2 patients and combined AR and mild AS in 1 patient. Twelve of the patients had predominant AS, which was qualified as severe in three, moderate in six and mild in three patients. Two patients had, in addition, AR, and one patient had moderate MS. Eight patients had pulmonic stenosis (PS), with a mean peak pressure gradient across the pulmonic valve of 59 ± 35 mm Hg (25 to 110 mm Hg).

Table 1 lists demographic information and baseline characteristics of the studied cases and their controls. There was a close match between the two groups in age, ethnicity, medical history, prenatal care, and the year of care. Obstetrical history was also identical except for higher number of previous abortions in patients with VHD (32 vs. 18, p = 0.017).

### All Patients

#### Maternal outcome.
Thirty-six (55%) of the VHD patients were in the NYHA functional class I; 28 (42%) were in class II, and 2 (3%) in class III on presentation. Heart disease was previously known in 25 class I patients, 16 class II patients, and 1 class III patient. Forty patients (62%) showed a deterioration of at least one functional class during pregnancy (Figs. 1 and 2), which occurred during the first trimester in 8 patients, second trimester in 26 patients and third trimester in 6 patients. Differences in maternal outcome between patients and controls are shown in Table 2. Patients with VHD demonstrated a significantly higher incidence of CHF, arrhythmias and hospitalizations during pregnancy. Thirty-four patients (52%) required cardiac medications during their index pregnancy, which included: diuretics, 27 patients; beta-blocking agents, 22 patients; calcium channel blockers, 13 patients; digoxin, 9 patients; potassium chloride, 7 patients; heparin, 4 patients; hydralazine, 1 patient; and aspirin, 1 patient. In 27 of these patients, therapy was either initiated or increased during pregnancy (first trimester, 8 patients; second trimester, 18 patients; third trimester, 1 patient).

In comparison, one patient in the control group was started on warfarin during pregnancy owing to deep-vein thrombosis. Mortality occurred in one valvular case and in none of the control cases (p = NS).

#### Mode of delivery.
Mode of delivery was vaginal in 61 of 66 (92%) cases with VHD and in 58 (87%) of controls (p = NS). Spontaneous vaginal delivery was reported in all 58 control cases but in only 38 (58%) of the patients (p = NS), whereas the remaining patients had either a forceps or vacuum delivery. Cesarean section was performed in eight control cases (all for obstetrical reasons) and in five VHD patients—two for cardiac reasons, including heart failure in one patient and acute ischemic syndrome in another.

### Postdelivery complications.
Pulmonary edema developed in three patients with MS (1 severe and 2 moderate) and in
two patients with moderate and severe AS post-delivery, and pneumonia developed in one patient with severe MS.

**Fetal outcome.** Information on fetal outcome is shown in Table 3. Stillbirth was reported in 3% of patients with VHD and in none of the controls ($p = NS$). Three percent of the patients had spontaneous abortions, and 5% had therapeutic abortions. Because information related to the control group was obtained retrospectively from delivery records, no data could be obtained regarding incidence of abortions in this population. A statistically significant difference occurred in the duration of pregnancy (35 ± 7 vs. 39 ± 2 weeks, $p = 0.0002$), in the incidence of premature deliveries, and in the incidence of intrauterine growth retardation (IUGR). In addition, birth weight was substantially lower in the patients when compared to controls. Six pregnancies lasted fewer than 32 weeks, and birth weight was ≤ the 10th percentile of the California Growth Curve in 13 cases with VHD and none in the controls ($p = NS$). The Apgar scores were <8 at 1 min in 9 of 66 patients and in 1 of 66 of the controls and at 5 min in 6 of 66 of patients and 0 of 66 of controls ($p = 0.588$).

**Subgroup Evaluation**

**Mitral stenosis.** There were 46 pregnancies in 44 patients with predominant MS. In 28 of these pregnancies, patients were in the NYHA functional class I on their first visit and 18 were in class II (Fig. 1). Thirteen class I patients advanced during pregnancy to class II, eight to class III and two to class IV. Seven class II patients advanced to class III and four to class IV. Both maternal and fetal outcomes were comparable in patients with mild MS and their control. In contrast, there was a significantly higher incidence of CHF, arrhythmias, need to initiate or increase dose of cardiac medications, and hospitalizations in patients with moderate and severe MS compared to their controls (Table 2). Despite high incidence of maternal morbidity, no mortality was reported in this group of patients. The effect of hemodynamically significant mitral valve disease on fetal outcome (Table 3) was reflected by a markedly increased rate of IUGR and lower birth weight. The incidence of preterm birth was higher in patients with mitral valve disease compared to controls; the difference, however, was not statistically significant ($p = 0.2$ for all MS patients and $p = 0.09$ for patients with moderate and severe MS).

**Aortic stenosis.** There were 12 pregnancies in 12 women with predominant AS. In five of these pregnancies, patients were in the NYHA functional class I on their first visit, five were in class II and two were in class III. Two class I patients advanced during pregnancy to class II, three class II patients advanced to class III and two class III patients advanced to class IV. There was a higher incidence of maternal CHF, arrhythmias, need to initiate or increase dose of cardiac medications, and hospitalizations in patients...
Table 2. Maternal Outcome in Patients With Valvular Heart Disease and Their Controls

<table>
<thead>
<tr>
<th>Valve Severity</th>
<th>CHF</th>
<th>Arhythmias</th>
<th>Medications</th>
<th>Hospitalizations</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
</tr>
<tr>
<td>Mitral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>11% 0% 0.5</td>
<td>0% 0% 1.0</td>
<td>5% 5% 1.0</td>
<td>11% 0% 0.5</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>61% 0% &lt; 0.01</td>
<td>22% 0% 0.1</td>
<td>72% 0% &lt; 0.01</td>
<td>61% 0% &lt; 0.01</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>Severe</td>
<td>78% 0% &lt; 0.05</td>
<td>33% 0% 0.23</td>
<td>100% 0% &lt; 0.02</td>
<td>78% 11% &lt; 0.1</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>All</td>
<td>43% 0% &lt; 0.0001</td>
<td>20% 0% &lt; 0.0001</td>
<td>50% 2%</td>
<td>43% 2% &lt; 0.001</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>Aortic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>33% 0% 1.0</td>
<td>0% 0% 1.0</td>
<td>33% 0% 1.0</td>
<td>0% 0% 1.0</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>17% 0% 1.0</td>
<td>0% 0% 1.0</td>
<td>33% 0% 1.0</td>
<td>17% 0% 1.0</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>Severe</td>
<td>100% 0% 0.5</td>
<td>33% 0% 1.0</td>
<td>33% 0% 1.0</td>
<td>67% 0% 0.5</td>
<td>33% 0% 1.0</td>
</tr>
<tr>
<td>All</td>
<td>42% 0% 0.06</td>
<td>8% 0% 1.0</td>
<td>33% 0%</td>
<td>25% 0% 0.2</td>
<td>8% 0% 1.0</td>
</tr>
<tr>
<td>Pulmonic</td>
<td>0% 0% 1.0</td>
<td>0% 0% 1.0</td>
<td>0% 0% 1.0</td>
<td>0% 0% 1.0</td>
<td>0% 0% 1.0</td>
</tr>
<tr>
<td>All patients</td>
<td>38% 0% &lt; 0.0001</td>
<td>15% 0% 0.001</td>
<td>41% 2% &lt; 0.001</td>
<td>35% 2% &lt; 0.001</td>
<td>2% 0% 1.0</td>
</tr>
</tbody>
</table>

CTRL = controls; PTS = patients.

with AS compared to their controls. Congestive heart failure was reported in 44% of patients with moderate and severe AS, arhythmias in 25%, new medications in 33%, and hospitalizations in 33% of patients. Because of the limited number of patients, incidence of CHF was only borderline statistically significant (p = 0.06), and differences in maternal morbidity between the two groups did not reach statistical significance. Similar to maternal outcome, fetal outcome also seemed to be affected by the presence of moderate and severe aortic valve disease as suggested by a higher incidence of preterm birth (44%), IUGR (22%), and lower birth weight (2650 ± 987 vs. 3391 ± 412 g, p = 0.002).

Table 3. Fetal Outcome in Patients With Valvular Heart Disease Versus Controls

<table>
<thead>
<tr>
<th>Valve Severity</th>
<th>Preterm Delivery</th>
<th>IUGR</th>
<th>Stillbirth</th>
<th>Birth Weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
<td>PTS CTRL p</td>
</tr>
<tr>
<td>Mitral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>5% (1/19) 11% (2/19) 1.0</td>
<td>16% (3/19) 0% (0/19) 0.6</td>
<td>0% (0/19) 0% (0/19) 1.0</td>
<td>3,135 ± 419 3,288 ± 531 0.3</td>
</tr>
<tr>
<td>Moderate</td>
<td>28% (5/18) 6% (1/18) 0.2</td>
<td>27% (5/18) 0% (0/18) 0.1</td>
<td>5% (0/18) 0% (0/18) 1.0</td>
<td>2,706 ± 1,039 3,427 ± 426 0.02</td>
</tr>
<tr>
<td>Severe</td>
<td>44% (4/9) 11% (1/9) 0.3</td>
<td>33% (3/9) 0% (0/9) 0.5</td>
<td>11% (0/9) 0% (0/9) 1.0</td>
<td>2,558 ± 947 3,332 ± 403 0.05</td>
</tr>
<tr>
<td>All</td>
<td>22% (10/46) 9% (4/46) 0.2</td>
<td>24% (11/46) 0% (0/46) &lt; 0.001</td>
<td>4% (0/26) 0% (0/26) 0.5</td>
<td>2,845 ± 818 3,372 ± 486 0.02</td>
</tr>
<tr>
<td>Aortic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>0% (0/3) 0% (0/3) 1.0</td>
<td>33% (1/3) 0% (0/3) 1.0</td>
<td>0% (0/3) 0% (0/3) 1.0</td>
<td>3,227 ± 843 3,083 ± 878 0.85</td>
</tr>
<tr>
<td>Moderate</td>
<td>33% (2/6) 0% (0/6) 0.5</td>
<td>33% (2/6) 0% (0/6) 0.5</td>
<td>0% (0/6) 0% (0/6) 1.0</td>
<td>2,450 ± 1,460 3,763 ± 511 0.08</td>
</tr>
<tr>
<td>Severe</td>
<td>66% (2/3) 0% (0/3) 0.5</td>
<td>0% (0/3) 0% (0/3) 1.0</td>
<td>0% (0/3) 0% (0/3) 1.0</td>
<td>1,838 ± 1,170 3,265 ± 141 0.2</td>
</tr>
<tr>
<td>All</td>
<td>0% (4/12) 0% (0/12) 0.1</td>
<td>25% (3/12) 0% (0/12) 0.2</td>
<td>0% (0/12) 0% (0/12) 1.0</td>
<td>2,752 ± 1,017 3,385 ± 694 0.09</td>
</tr>
<tr>
<td>Pulmonic</td>
<td>12% (1/8) 0% (0/8) 1.0</td>
<td>25% (1/8) 0% (0/8) 1.0</td>
<td>0% (0/8) 0% (0/8) 1.0</td>
<td>3,376 ± 565 3,300 ± 429 0.8</td>
</tr>
<tr>
<td>All patients</td>
<td>23% (15/66) 6% (4/66) 0.03</td>
<td>21% (14/66) 0% (1/66) 0.0001</td>
<td>3% (0/26) 0% (0/26) 0.5</td>
<td>2,897 ± 838 3,365 ± 515 &lt; 0.001</td>
</tr>
</tbody>
</table>

CTRL = controls; IUGR = intrauterine growth retardation; PTS = patients.
presentation. None of the patients showed a significant deterioration during pregnancy (Fig. 2). In addition, there were no hospitalizations, arrhythmias, or need to initiate cardiac medications in this group during gestation (Table 2), and all pregnancies resulted in a live birth. One preterm birth and one case of IUGR occurred compared to none in the controls (Table 3). Differences between the groups, however, were not statistically significant. Mean birth weight was similar in the two groups.

**DISCUSSION**

The results of the present study demonstrate a significant impact of VHD on both maternal and fetal outcome.

**Maternal outcome.** Women with VHD had a high rate of clinical deterioration and a marked increase in morbidity events during pregnancy, including CHF, arrhythmias and need to either initiate or increase cardiovascular drug therapy or to hospitalize patients during pregnancy. An increased incidence of CHF in patients with VHD is not surprising owing to the marked hemodynamic changes normally occurring during gestation (6). Increased hemodynamic burden during gestation is also a possible mechanism for new onset or worsening of existing arrhythmias observed in this study in women with VHD. Increased incidence of cardiac arrhythmias has also been described in healthy women during pregnancy (7–11), and this may be related to gestational hormonal effect and a possible increased sensitivity to catecholamines during gestation (12). Such arrhythmias, however, are uncommon, and they were not reported in any of the women in the control group.

**Fetal outcome.** In addition to the effect on maternal morbidity, the present study also demonstrated an effect of VHD on fetal outcome. Pregnancy in our patients was associated with an increased incidence of IUGR, preterm deliveries, and lower birth weight, especially in cases with moderate and severe stenosis of the mitral or aortic valve. Hemodynamic compromise secondary to valvular stenosis and the resulting decrease in uterine blood flow are probable explanations for the high incidence of impaired intrauterine fetal growth seen in this study of patients with VHD.

In addition, maternal arrhythmias have been shown to cause fetal distress (10) and may be an additional mechanism leading to compromised uterine blood flow and fetal outcome. Although the fetal effect of cardiovascular drugs used in many of the patients cannot be assessed, such medications, including diuretics, digitalis, and beta-adrenergic blocking agents, have been associated with impairment of uterine blood flow or with increased incidence of IUGR or prematurity (13–17). The increased incidence of IUGR shown in this study suggests the need for antepartum fetal surveillance and serial ultrasound determinations of fetal growth in all cases of moderate and severe aortic and mitral valve disease.

**Relation to type and severity of VHD.** Although subgroup analysis of our findings may be limited owing to a relative small number of patients in each subgroup, a clear relationship can be found between the severity of MS and AS and maternal as well as fetal outcome. Though the overall incidence of complications was high in patients with moderate and severe disease, the outcome of pregnancy in most patients with mild MS and AS was comparable to that of their normal controls.

Despite the relative severity of PS in our patients, pregnancy was well tolerated and outcome was comparable to that seen in their control patients. Although this finding supports previously reported clinical experience (18–20), the number of patients with PS in the present study was small and the results cannot be conclusive.

**Maternal mortality.** Despite a high incidence of maternal morbidity, mortality was limited to one patient (2%) with severe AS combined with coarctation of the aorta. Furthermore, because mortality occurred in the postpartal period (1), 10 days following a successful abdominal delivery and in conjunction with surgery for aortic valve replacement, the association between this patient’s death and pregnancy was questionable. Our data, supported by other reports (4,21,22), indicate, therefore, that with early diagnosis and careful follow-up, mortality is rare in medically treated patients with VHD at NYHA functional class I and II.

**Valvular repair during pregnancy.** Valvular repair, either surgically or by percutaneous balloon valvuloplasty, is the procedure of choice in symptomatic, nonpregnant patients with VHD. Successful cardiovascular surgery has been reported during pregnancy (23,24). The overall experience, however, suggests a moderate increase in maternal risk and an unpredictable risk to the fetus or neonate (24,25). The use of percutaneous balloon valvuloplasty during pregnancy has been reported in patients with both mitral and aortic stenosis (26–31). A recent study by Ben Farhat et al. (27) reported on forty-four pregnant patients who underwent percutaneous balloon valvuloplasty of the mitral valve between 1990 and 1996 with a significant hemodynamic benefit and a favorable pregnancy outcome. These data compare favorably to our findings and may support the use of percutaneous balloon valvuloplasty during pregnancy in patients with moderate to severe MS. At the same time, however, important valvuloplasty-related complications including cardiac tamponade, systemic embolization, maternal arrhythmias, initiation of uterine contractions, fetal distress and fetal loss have been reported (27,30–32). These potential complications, in addition to fetal risk due to unavoidable ionizing radiation (33), indicate the need for additional data and appropriate, controlled comparison with medical therapy before widespread use of percutaneous balloon valvuloplasty can be recommended during pregnancy.

**Mode of delivery.** The majority of patients with VHD as well as their controls were delivered vaginally. Although a high incidence of vaginal delivery in this study reflects practice approach in our institution, these findings indicate
that cesarean section, which is often performed as a preferred delivery method in patients with heart disease, should be reserved for patients with obstetrical indications or cardiac instability.

Postdelivery complications. Development of pulmonary edema in five patients early postdelivery is most likely related to increased venous return due to relief of inferior caval compression (7). These findings suggest a rationale for close hemodynamic monitoring during labor, delivery, and the early postpartum period in patients with significant valvular stenosis.

Summary and clinical implications. The present study demonstrates an important effect of VHD on both maternal and fetal outcome of pregnancy. Increased maternal morbidity was reflected by clinical deterioration in more than half of the patients, high incidence of CHF and cardiac arrhythmias, and the need either to initiate or enhance cardiovascular drug therapy and to hospitalize many of the patients during pregnancy. Maternal mortality was low and occurred in only one patient with severe AS and coarctation (<2%) after surgery. In addition, presence of maternal VHD had an important effect on fetal outcome, leading to increased incidence of IUGR, premature labor, and decreased birth weight. The effect of VHD on pregnancy outcome was seen mostly in patients with moderate and severe AS and MS, whereas only little or no effect was noted in patients with mild degree of these conditions and in those with PS.

Finally, the results of this study indicate the need for close maternal follow-up and fetal surveillance in pregnant patients with moderate or severe AS and MS. Repair of valvular stenosis in such patients should be performed prior to pregnancy, if possible. Balloon valvuloplasty should be considered during pregnancy in order to prevent maternal and fetal complications. The possible benefits of this procedure, however, should be carefully weighed against its potential risks during pregnancy.

APPENDIX

Abortio n is the termination of pregnancy by any means before the fetus is sufficiently developed to survive. In the United States this definition is confined to the termination of pregnancy before 20 weeks based on the date of the first day of the last normal menses.

Preterm is defined as infants delivered prior to the completion of 37 weeks (American College of Obstetricians and Gynecologists, 1995).

Intrauterine growth retardation. This term is used synonymously as small for gestational age (SGA) infants are those whose weights are below the 10th percentile for their gestational age. (Lubchenco LO, Hansman C, Dressler M, Boyd E. Intrauterine growth as estimated from live-born birth-weight data at 24 to 42 weeks of gestation. Pediatrics 1963;32:793.)

Stillbirth. None of the signs of life are present at or after birth. (Williams Obstetrics. 20th ed. Appleton & Lange, 1997).

REFERENCES