Hypertrophic cardiomyopathy in South African Blacks

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Summary

Hypertrophic cardiomyopathy (HCM) has been considered rare among the Black population of southern Africa. We report 7 patients with the disease who presented during a 14-month period. Current concepts in the approach to the diagnosis and treatment of HCM are discussed. It is possible that with greater awareness of the occurrence of the condition in Blacks the diagnosis of HCM will be made in more members of this population group.

S Afr Med J 1983; **63**: 266-269

Hypertrophic cardiomyopathy (HCM) is an important cardiac lesion to diagnose. Although some patients are asymptomatic, others complain of angina pectoris, syncope or shortness of breath, and sudden death may occur.[1] The disease is often familial, inherited as a mendelian dominant gene with variable penetrance.[2]

HCM is not uncommon among White South Africans[3] but only 4 Black HCM patients have been reported,[4,5] and the disease has been considered to be rare in this racial group. We report 7 Black patients with HCM seen in the Division of Cardiology, Baragwanath Hospital, over a 14-month period, in order to draw attention to the condition in South African Blacks. The diagnosis and current concepts of the pathophysiology and management of HCM are discussed.

Patients and methods

The clinical data are summarized in Table I. All patients claimed to be of pure Black descent. They belonged to different Bantu tribes: there were 3 Tswanas, 2 Xhosas and 1 each of Zulu and Venda origin. Five of the 7 were males and all were young (age range 19-38 years). Anginal-type chest pain was the presenting symptom in 5 patients. One patient claimed to be asymptomatic except for having had two episodes of acute breathlessness, for which he was admitted to hospital with pulmonary oedema. The 7th patient was asymptomatic and had been referred for evaluation of a harsh systolic murmur detected during routine physical examination for insurance purposes. The duration of symptoms varied, but only 1 (patient 5) had a history exceeding 2 years.

Physical examination revealed left ventricular hypertrophy (LVH) in all patients, with a prominent presystolic impulse at the apex in 6. A 'jerky', rapidly rising pulse was readily apparent in 4. The splitting of the second heart sound was abnormally narrow or partially reversed[3] in all 7 patients. All had a delayed onset systolic ejection murmur; this increased in intensity on standing and became softer on squatting in 3. The ECG showed severe LVH with T-wave inversion over the left ventricle in all patients, in 4 of whom deep septal Q waves were also present. In only one instance (patient 5) was the heart enlarged as seen on radiography, but all 7 had a shelf-like outline to the left heart border which gave the left ventricle a 'bulky' appearance compatible with LVH (Fig. 1). Signs of pulmonary venous hypertension were present in 4 patients.

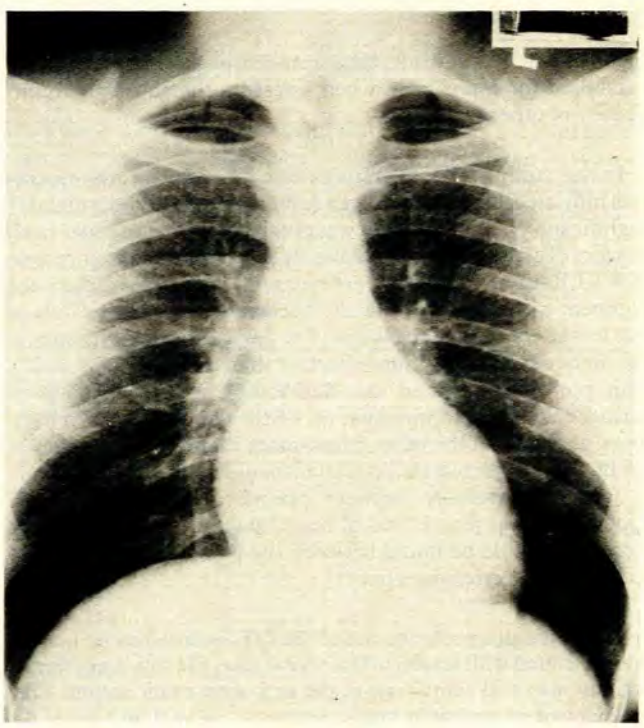

Fig. 1. Postero-anterior chest radiograph of patient 7. The cardiothoracic ratio is 0,50 but there is a prominent shelf-like appearance to the left heart border which gives the left ventricle a 'bulky' appearance, and is compatible with LVH.

Echocardiography was diagnostic of HCM in all patients (Table II). In 5 both M-mode and high quality real-time two-dimensional echocardiograms were recorded, whereas in the remaining 2 (patients 2 and 3) the M-mode technique only was available. Echocardiography showed severe LVH (Fig. 2) in all patients; the hypertrophy was asymmetrical, mainly involving the septum, in 5. Systolic anterior motion (Fig. 3) of the anterior mitral leaflet was present in these 5 patients, in 3 of whom midsystolic closure of the aortic valve was also seen.

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TABLE I. CLINICAL, ELECTROCARDIOGRAPHIC AND RADIOGRAPHIC FINDINGS

Patient	Age (yrs)	Sex	Race	Presenting symptoms	Duration of symptoms	Disability*	ECG	Chest radiograph
1	28	M	Tswana	Chest pain, palpitations, shortness of breath	2 yrs	2b	Severe LVH, deep septal Q waves	CTR 0,45, 'bulky' LV, pulmonary venous hypertension
2	19	M	Zulu	Chest pain	1 yr	2a	Severe LVH, prominent Q waves in leads I and V3-V6	CTR 0,50, 'bulky' LV
3	19	M	Xhosa	Chest pain, palpitations	6 mo.	2a	Severe LVH, septal Q waves in leads I and aVL	CTR 0,48, 'bulky' LV, pulmonary venous hypertension
4	32	M	Xhosa	Two episodes of pulmonary oedema. Otherwise 'asymptomatic'	2 yrs	1	Severe LVH	CTR 0,50, 'bulky' LV, intermittent pulmonary oedema
5	30	F	Tswana	Chest pain	10 yrs	2a	Severe LVH	CTR 0,63, 'bulky' LV, pulmonary venous hypertension
6	35	F	Tswana	Chest pain, palpitations, shortness of breath	2 yrs	2b	Severe LVH	CTR 0,52 'bulky' LV, LA+, pulmonary venous hypertension
7	38	M	Venda	Asymptomatic	—	1	Severe LVH, deep septal Q waves	CTR 0,50, 'bulky' LV

*New York Heart Association grading.
CTR = cardiothoracic ratio; LV = left ventricle; LVH = left ventricular hypertrophy; LA+ = left atrial enlargement.

TABLE II. ECHOCARDIOGRAPHIC, HAEMODYNAMIC AND ANGIOGRAPHIC DATA

		Cardiac pressures (mmHg)			
		Left ventricle (apex) systolic			
Patient	Echocardiography	y,z,a	Peak systolic gradient	Angiography	EF (%)
1	Severe LVH with small cavity, ASH, SAM of anterior mitral leaflet, midsystolic aortic leaflet closure	180 / 10,14,22	80	Severe LVH with septal hypertrophy, trivial MI	87
2	Severe LVH	200 / 6,10,20	50	Severe LVH; mild MI	85
3	Severe LVH with small cavity, ASH, SAM of anterior mitral leaflet	140 / 2,4,10	40	Severe LVH	78
4	Severe LVH	150 / 4,6,11	0	Severe LVH	80
5	Severe LVH with ASH, SAM of anterior mitral leaflet, midsystolic aortic leaflet closure	—	—	—	—
6	Severe LVH with small cavity, ASH, SAM of anterior mitral leaflet	125 / 0,8,12	10 (35 on isoprenaline)	Severe LVH, small cavity and septal bulge	94
7	Severe LVH with small cavity, ASH, SAM of anterior mitral leaflet, midsystolic aortic valve closure	200 / 5,12,24	100	Severe LVH, small cavity and septal bulge	84

ASH = asymmetric septal hypertrophy; SAM = systolic anterior motion; MI = mitral incompetence; EF = ejection fraction.

Cardiac catheterization (Table II) was performed in all except patient 5. The left ventricular end-diastolic pressure was increased in 3, and in all 6 a prominent 'a' wave was recorded in this chamber. An intraventricular pressure gradient was present in 5 patients, but in the 6th there was no pressure difference at rest, after an ectopic beat or during isoprenaline infusion. In all 6 left ventricular angiography confirmed marked LVH and showed vigorous myocardial contraction with a markedly increased ejection fraction and a small left ventricular cavity. There was almost complete cavity obliteration of the ventricle in 4 of the 6 patients.

The patients were treated with a ß-adrenergic blocking drug, with the addition of the calcium antagonist verapamil in patients 1 and 7. Symptoms improved in all, but patient 1 continues to complain of chest pain.

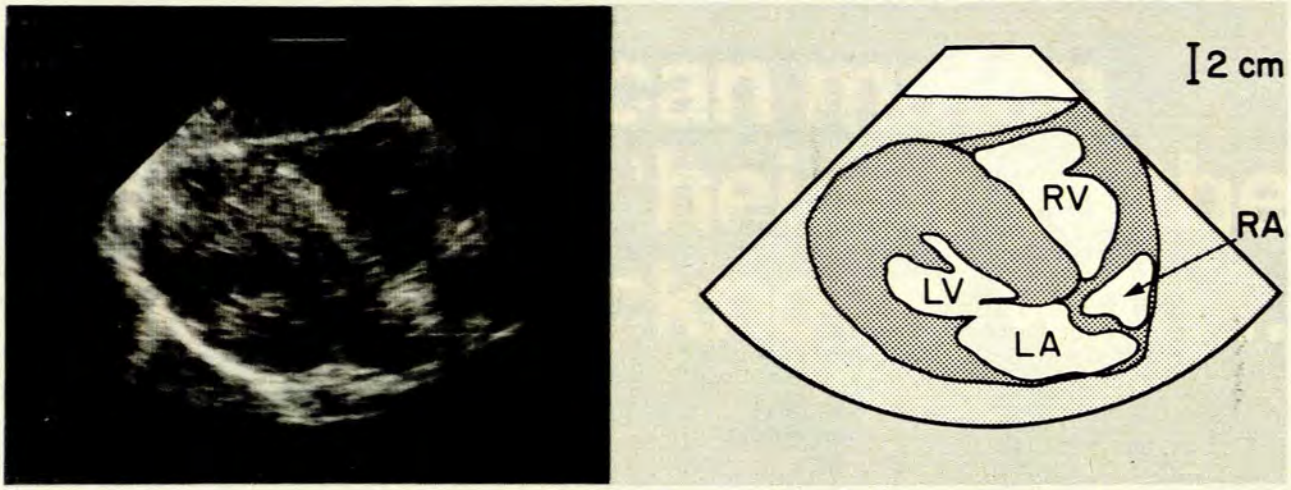

Fig. 2. Real-time two-dimensional echocardiogram (subxiphoid four-chamber view) of patient 7 (end-diastolic frame). There is marked LVH, especially of the interventricular septum. The left ventricular cavity is small (RV = right ventricle, LV = left ventricle, LA = left atrium, RA = right atrium).

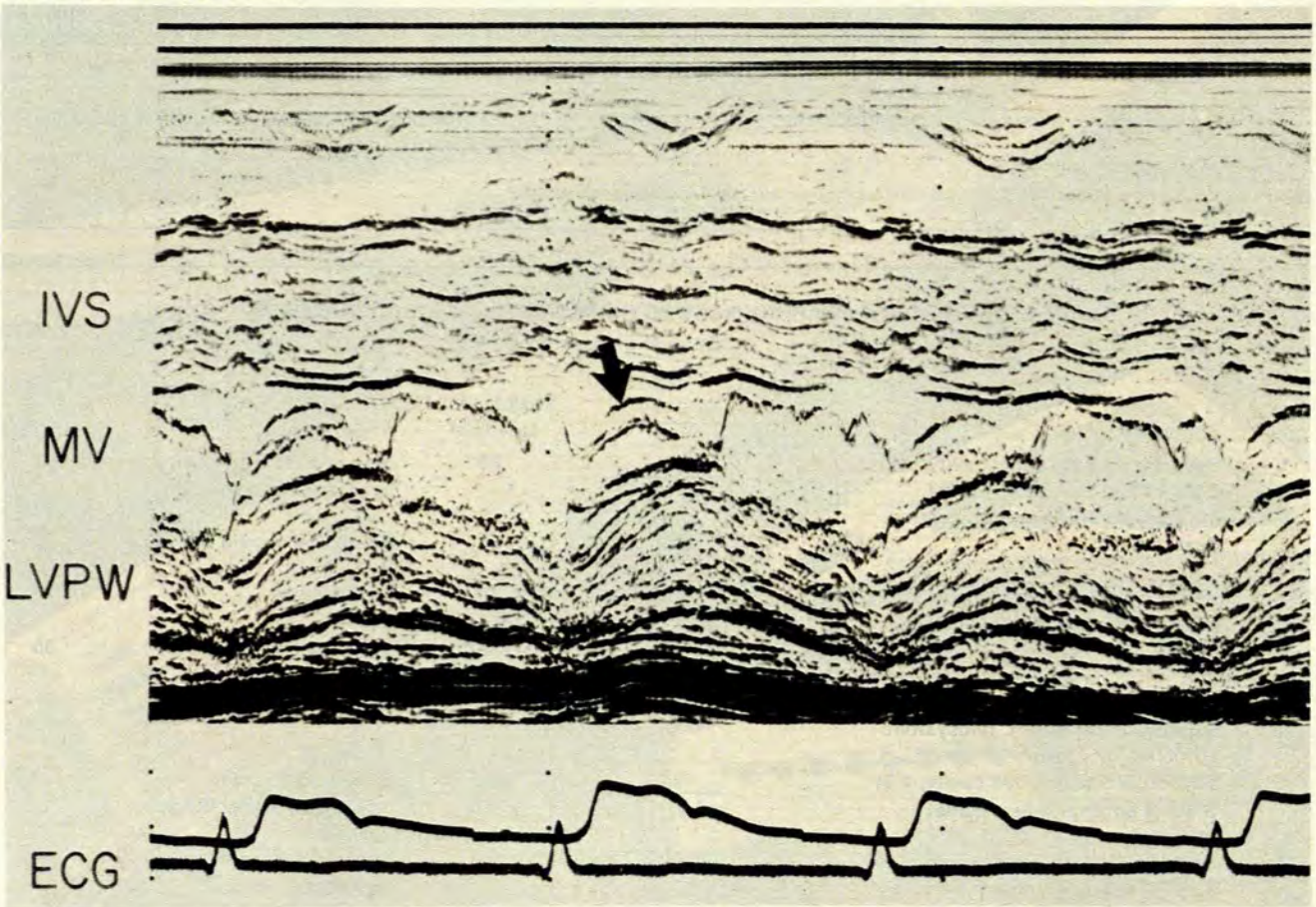

Fig. 3. M-mode echocardiogram (patient 1), showing considerable hypertrophy of the left ventricular posterior wall (LVPW) and especially of the interventricular septum (IVS). The anterior leaflet of the mitral valve (MV) shows abnormal systolic anterior motion (arrowed). This coincides with a systolic notch in the carotid pulse tracing recorded simultaneously with the ECG.

Discussion

Pathophysiology of HCM

In HCM there is inappropriate and sometimes considerable hypertrophy of the ventricular myocardium, predominantly affecting the left ventricle. The excessive LVH has two principal consequences: (*i*) ventricular relaxation and compliance are abnormal, diastolic ventricular stiffness is increased, ventricular filling is impaired and the end-diastolic pressure may be elevated; and (*ii*) myocardial contraction is more forceful and the distorted left ventricular cavity may produce an intraventricular pressure difference during systole, but this is not an invariable feature of the condition.[6] The symptoms of HCM include *angina pectoris* (due to increased myocardial oxygen demand and a diminished diastolic coronary perfusion gradient), *dyspnoea* (the clinical manifestation of the raised left ventricular end-diastolic and left atrial pressures) and *syncope* (probably mainly due to

arrhythmias, but aggravated by the small left ventricular cavity size which limits the stroke output). *Sudden death* may supervene, especially during exercise or with emotion.

The pathogenesis of the inappropriate LVH is unknown. There may be an inherited malformation of muscle in different parts of the myocardium with fibre malalignment, resulting in abnormal ventricular stresses and excessive hypertrophy.[7] The distribution of the abnormal regions would determine the precise geometry of the left ventricular cavity in a particular patient,[8] and where there is marked septal hypertrophy the so-called 'obstructive' form of the disease usually results. In most patients this 'obstruction' (as seen on angiography or echocardiography) is subvalvar, but in a few instances it is midventricular[9] (hour-glass type). Hypertrophy confined to the apical myocardium, giving a typical 'spade-like' appearance on angiography, has been emphasized by Japanese workers.[10] It has been argued,[11,12] however, that the pressure difference within the left ventricular cavity does not reflect a true obstruction to left ventricular emptying, but that rapid ejection during early systole and cavity obliteration can account for many of the haemodynamic, echocardiographic and angiographic features hitherto attributed to 'obstruction'.[11]

Diagnostic features of HCM

The diagnosis of HCM should be suspected in any patient who has inappropriate, unexplained LVH. The arterial pulse often has a rapid upstroke, in contrast to the slow-rising pulse of aortic stenosis, since in HCM early systolic ventricular emptying is normal or increased. A second pulse wave, producing a bisferiens character, may be felt in late systole. On auscultation a delayed onset systolic murmur is almost always present, and this murmur changes characteristically with various haemodynamic alterations.[3] Splitting of the second heart sound is abnormal and the pattern of the splitting, whether narrow, reversed or partially reversed, changes spontaneously within seconds and without apparent cause.[3] The ECG is seldom normal and commonly suggests severe LVH. Deep septal Q waves may be present, especially in patients with excessive septal hypertrophy. Electrocardiographic evidence of unexplained LVH should always raise the possibility of HCM. The chest radiograph not infrequently shows only slight or even no cardiac enlargement as assessed by the cardiothoracic ratio. However, in our experience a shelf-like appearance to the left heart border is characteristic of HCM, and the diagnostic importance of this sign (Fig. 1) was confirmed in the present series.

The echocardiogram is diagnostic in HCM and has probably obviated the need for cardiac catheterization in most patients. The echocardiogram, and especially the real-time two-dimensional echocardiogram, shows the distribution and degree of LVH, the forceful contraction of the left ventricle with cavity obliteration, and the systolic anterior motion of the mitral valve which is present in some patients and is attributed to asymmetrical tension on the mitral apparatus by the distorted left ventricular geometry. Midsystolic fluttering and closure of the aortic leaflets are usually associated with a significant intraventricular pressure gradient.

Management of HCM

The medical management of patients with HCM is aimed at decreasing left ventricular contractility and increasing ventricular compliance and cavity size. Beta-receptor blockade[13-15] improves the haemodynamic state and is effective in the treatment of symptoms. The calcium antagonist verapamil[16] also improves symptoms in many patients, and may decrease LVH after long-term use. Using large doses of propranolol in conjunction with anti-arrhythmic drugs and pacemakers, Canedo and Frank[15] were able to reduce the overall mortality rate of patients with HCM to 0,5% per year. Since even asymptomatic patients are at risk of sudden death, all patients with HCM should be given a ß-blocker or calcium antagonist at adequate dosage and should undergo regular Holter monitoring in order to detect and treat potentially life-threatening arrhythmias. Echocardiography is a useful screening test for HCM, and should be used to detect HCM in family members of patients with the disease.

In patients with large intracavitary gradients surgical intervention (extensive left ventricular myectomy) may be indicated. Although good results have been reported,[17] it is not clear whether this alters the long-term prognosis of the disease.

HCM in southern Africa

HCM is not uncommon in South African Whites,[3] but for many years was not recognized in the Black population. The disease may be less common in South African Blacks since there is a strong genetic factor. HLA typing has shown distinct trends in the HLA patterns of patients with HCM, but the patterns vary in different ethnic groups.[18,19] HCM certainly occurs in North American Blacks, and it is possible that many Black patients in southern Africa have not been diagnosed because of having nonspecific, relatively minor symptoms or signs. Screening of a large number of subjects in this population by means of electrocardiography, radiography and echocardiography may enable more cases to be diagnosed. The problem of diagnosis is compounded by the fact that very large numbers of seriously ill Black patients are examined and treated in southern Africa. In this context patients with minor or atypical complaints (such as many patients with HCM have) either do not consult a medical practitioner or may not be referred to a specialist centre. Moreover, congestive cardiomyopathy is very common in this population, and it is possible that some patients with unexplained cardiac symptoms or cardiac enlargement are loosely diagnosed as having 'cardiomyopathy' without further investigation or referral. The fact that during the last 14 months we have seen 7 patients with severe HCM identical to that seen elsewhere in the world and to that occurring in White South Africans suggests that the disease is not as rare in this group as has been thought. A greater awareness of the condition may reveal more cases of HCM in the South African Black population.

This study was supported in part by the Stella and Paul Loewenstein Cardiac Fund of the University of the Witwatersrand.

REFERENCES

1. Maron BJ, Roberts WC, McAllister HA, Rosing DR, Epstein SE. Sudden death in young athletes. *Circulation* 1980; **62:** 218-229.
2. Braunwald E, Lambrew CT, Rockoff SD, Ross J jun, Morrow AG. Idiopathic hypertrophic subaortic stenosis. *Circulation* 1964; **30:** suppl IV, 3.
3. Tucker RBK, Zion MM, Pocock WA, Barlow JB. Auscultatory features of hypertrophic obstructive cardiomyopathy. *S Afr Med J* 1975; **49:** 179-186.
4. Nellen M. In: Wolstenholme GEW, O'Connor M, eds. *Hypertrophic Obstructive Cardiomyopathy* (Ciba Foundation Study Group Report No. 37). London: J & A Churchill, 1971: 42.
5. Lewis BS, Armstrong TG, Mitha AS, Gotsman MS. Hypertrophic obstructive cardiomyopathy in the South African Bantu. *S Afr Med J* 1973; **47:** 599-604.
6. Goodwin JF, Oakley CM. The cardiomyopathies. *Br Heart J* 1972; **34:** 545-552.
7. Ferrans VJ, Morrow AG, Roberts WC. Myocardial ultrastructure in idiopathic hypertrophic subaortic stenosis. *Circulation* 1972; **45:** 769-792.
8. Olsen EGJ. *The Pathology of the Heart.* London: Macmillan, 1980: 317.
9. Falicov RE, Resnekov L. Mid-ventricular obstruction in hypertrophic obstructive cardiomyopathy. *Br Heart J* 1977; **39:** 701-705.
10. Yamaguchi H, Ishimura T, Nishiyama S *et al.* Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. *Am J Cardiol* 1979; **44:** 401-412.
11. Criley JM. The bottom line syndrome: hypertrophic cardiomyopathy revisited. *West J Med* 1979; **130:** 350-353.
12. Goodwin JF. Hypertrophic cardiomyopathy: a disease in search of its own identity. *Am J Cardiol* 1980; **45:** 177-180.
13. Webb-Peploe MM, Croxson RS, Oakley CM, Goodwin JF. Cardioselective beta-adrenergic blockade in hypertrophic obstructive cardiomyopathy. *Postgrad Med J* 1971; **47:** suppl, 93-97.

14. Lewis BS, Mitha AS, Bakst A, Purdon KL, Gotsman MS. Haemodynamic effects of beta blockade in hypertrophic cardiomyopathy using Sectral (acebutolol, M & B 17803A). *Cardiovasc Res* 1974; **8:** 249-262.
15. Canedo MI, Frank MJ. Therapy of hypertrophic cardiomyopathy: medical or surgical? Clinical and pathophysiologic considerations. *Am J Cardiol* 1981; **48:** 383-388.
16. Kaltenbach M, Hopf R, Kober G, Bussman WD, Keller M, Petersen Y. Treatment of hypertrophic obstructive cardiomyopathy with verapamil. *Br Heart J* 1979; **42:** 35-42.
17. Maron BJ, Merrill WH, Freier PA, Keet KM, Epstein SE, Morrow AG. Long-term clinical course and symptomatic status of patients after operation for hypertrophic subaortic stenosis. *Circulation* 1978; **57:** 1205-1213.
18. Darsee JR, Heymsfield SB, Nutter DO. Hypertrophic cardiomyopathy and human leukocyte antigen linkage: differentiation of two forms of hypertrophic cardiomyopathy. *N Engl J Med* 1979; **300:** 877-882.
19. Matsumori A, Kawai C, Wakabayashi A *et al.* HLA-DRW4 antigen linkage in patients with hypertrophic obstructive cardiomyopathy. *Am Heart J* 1981; **101:** 14-16.