

REVIEW

Metabolic Syndrome and Cardiovascular Risk: The Nurse's Role

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ABSTRACT

Metabolic Syndrome (MS) is characterized by dysglycemia, arterial hypertension, atherogenic dyslipidemia and central obesity. Its presence has been associated with increased risk for the development of diabetes mellitus and cardiovascular disease. The main treatment goal is to lower the incidence of both MS and its cardiovascular sequelae and includes diet, exercise, weight loss, control of blood glucose and pharmacological therapy of hypertension and dyslipidemia. Nursing care focuses in the development of a concise treatment plan based upon patient's education, psychosocial support and close follow-up. Nurses should have a wide knowledge of MS pathophysiology which will facilitate their active participation in both diagnosis and treatment processes. The final goal is to assure the long-term compliance of patients with both the proposed lifestyle changes and the medical treatment in order to achieve a significant reduction in their cardiovascular morbidity and mortality.

KEY WORDS: *metabolic syndrome; diabetes mellitus; obesity; hyperlipidemia; hypertension; nursing intervention*

INTRODUCTION - HISTORY

The clustering of cardiovascular risk factors like obesity, type 2 diabetes, hyperlipidemia and hypertension in the same person was initially described several decades ago.^{1,2} On the other hand, insulin resistance has been the earliest described characteristic of type 2 diabetes mellitus.³ The association of diabetes with hyperinsulinemia, hyperlipidemia, obesity and hypertension were subsequently reported. Thus, it became clear that the majority of patients suffering from type 2 diabetes had also high incidence of several other cardiovascular risk factors.⁴ This risk factor clustering and its association with insulin resistance was attributed to a distinct pathophysiologic entity named initially as "insulin resistance syndrome".^{5,6}

Reaven in his hallmark lecture in 1988⁷ unified and expanded these aspects by introducing the term "syndrome X" to describe the combination of these cardiovascular risk factors (hypertension, hyperglycemia, dyslipidemia). He developed the hypothesis that insulin resistance resulting in compensatory increased insulin plasma levels, predisposed to the development of hypertension, hyperlipidemia and diabetes. Obesity was not included in Reaven's list of insulin resistance derived abnormalities although he accepted the existence of an association between obesity and insulin resistance. Subsequently, other investigators underlined the pivotal role of obesity as

LIST OF ABBREVIATIONS:

MS= metabolic syndrome
BMI= body mass index
HDL= high density lipoprotein
LDL= low density lipoprotein

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a causal factor of Reaven's syndrome X and used instead the term "Metabolic Syndrome" (MS) which finally prevailed in the literature and in clinical practice.⁸

DEFINITION AND PATHOPHYSIOLOGY OF THE METABOLIC SYNDROME

Metabolic Syndrome is a combination of interrelated metabolic abnormalities (*metabolic risk factors*) that increase the risk of atherosclerotic cardiovascular disease. Patients with MS are prone to the development of diabetes mellitus type 2, coronary artery disease and cerebrovascular disease. Another cluster of pathophysiologic conditions (*underlying risk factors*) are thought to be the cause of the metabolic risk factors. Dyslipidemia, high blood pressure and high blood glucose are the principal metabolic risk factors. Patients with these abnormalities are also frequently in a pro-thrombotic and pro-inflammatory state.⁹⁻¹¹

The most important underlying risk factors are central obesity and insulin resistance, whereas associated conditions are sedentary life, age and hormonal abnormalities leading to increased androgen production (e.g. polycystic ovary syndrome) (Fig. 1).¹²⁻¹⁴ Although the cause of MS has not been clearly defined, most experts agree that insulin resistance is the primary underlying abnormality.¹⁵ Insulin resistance is responsible for the hyperglycemia observed in diabetes mellitus. Multiple metabolic pathways have been proposed as the link between insulin resistance, compensatory hyperinsulinemia and the other metabolic risk factors.¹⁶ On the other hand, insulin resistance is closely related to the development of abdominal or central obesity which is thought to be responsible for the increased prevalence of the MS noted during the last few years. Individuals with insulin resistance are not necessar-

ily overweight. They exhibit however an abnormal distribution of adipose tissue mainly in the upper part of their body (central obesity).¹⁷ This type of obesity highly correlates with insulin resistance.¹⁸ Interestingly, upper body fat distribution leads to an increased release of non-esterified fatty acids from the adipose tissue in the circulation which subsequently accumulate in other tissues.^{19,20} This ectopic fat accumulation into the muscles²¹ and the liver²² –the two main target organs of insulin- predispose to insulin resistance. Moreover, the abnormal production of fatty tissue hormones (adipokines) also affect insulin sensitivity and modifies atherosclerosis risk factors like inflammatory cytokines and tissue plasminogen activator inhibitor.^{23,24} Based on these findings some investigators believe that a low-grade inflammation may be either the underlying cause or simply the aggravating factor of the MS.^{25,26} Finally some genetic predisposition to the development of the MS is also thought to exist. This genetic background seems to influence the phenotypic expression of the syndrome after exposure in different environments. This seems to explain the ethnic variations in the clinical expression of metabolic risk factors in obese individuals with insulin resistance.²⁷

Several terms, other than MS, have been proposed in the literature, such as Dysmetabolic or Polymetabolic Syndrome, Insulin Resistance Syndrome, or Syndrome X. Three definitions of the MS are currently in common use. According to the World Health Organization's (WHO)²⁸ diagnostic criteria, dysglycemia (diabetes, glucose intolerance) along with two of the following, increased body mass index (BMI), dyslipidemia, high blood pressure and microalbuminuria, are required to define the MS (Fig. 2). The National Cholesterol Education Program Adult Treatment Program III (NCEP ATP III)²⁹ criteria are more suitable for clinical use although based upon the same principle (Fig. 3). At least three of the following criteria

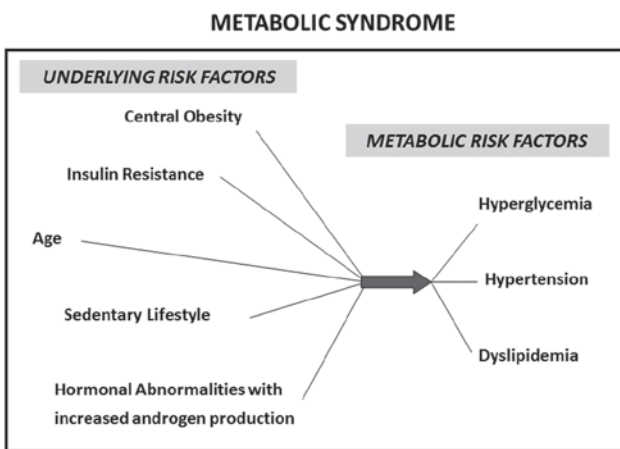


FIGURE 1. Metabolic risk factors and their underlying abnormalities in the metabolic syndrome.

DEFINITION OF THE METABOLIC SYNDROME
IDF (International Diabetes Federation)

- Central obesity (waist circumference ≥ 94 cm men, ≥ 80 cm women)

and 2 or more from:

- ✓ Triglycerides ≥ 150 mg/dl or specific treatment for hypertriglyceridemia
- ✓ HDL cholesterol < 40 mg/dl men, < 50 mg/dl women or specific treatment for low HDL cholesterol
- ✓ Arterial blood pressure $\geq 130 / 85$ mm Hg or antihypertensive treatment
- ✓ Fasting glucose ≥ 100 mg/dl or previously diagnosed type 2 diabetes mellitus

FIGURE 2. Definition of the metabolic syndrome (MS) according to the World Health Organization (WHO) criteria.

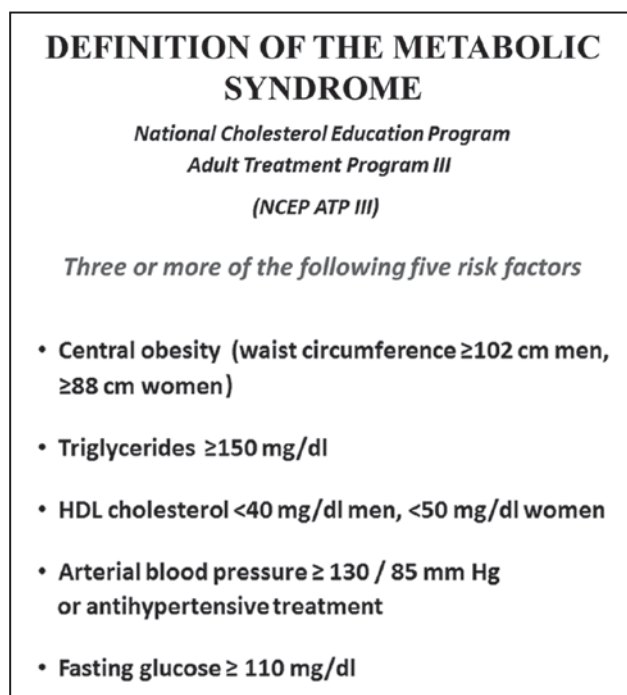


FIGURE 3. Definition of the metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Program III (NCEP ATP III) criteria.

have to be present: central obesity, dyslipidemia, hypertension, and fasting glucose ≥ 110 mg/dl. In the most recent definition of MS published by the International Diabetes Federation (IDF)³⁰ (Figure 4), fasting glucose cut-off point have been lowered to 100 mg/dl. Central obesity in addition to two of the other classic criteria is required for the diagnosis.

**METABOLIC SYNDROME AND
CARDIOVASCULAR RISK – PREVALENCE
OF THE METABOLIC SYNDROME**

Every single component of the MS increases cardiovascular risk,³¹⁻³³ while their combination has been associated with an exponential increase of cardiovascular morbidity and mortality.³⁴⁻³⁶ Many studies have shown that patients with MS have an increased incidence of cardiovascular disease. In these studies, the risk excess varies from 30-400%. This high variability could be attributed to differences in the populations studied, in the definition criteria used and in the follow-up time. From a pathophysiologic point of view, insulin resistance has been related to endothelial dysfunction³⁷ and to a delayed clearance of atherogenic lipoproteins in the postprandial state³⁸ promoting this way the development of the atherosclerotic plaque. Obesity, on the other hand, has been associated

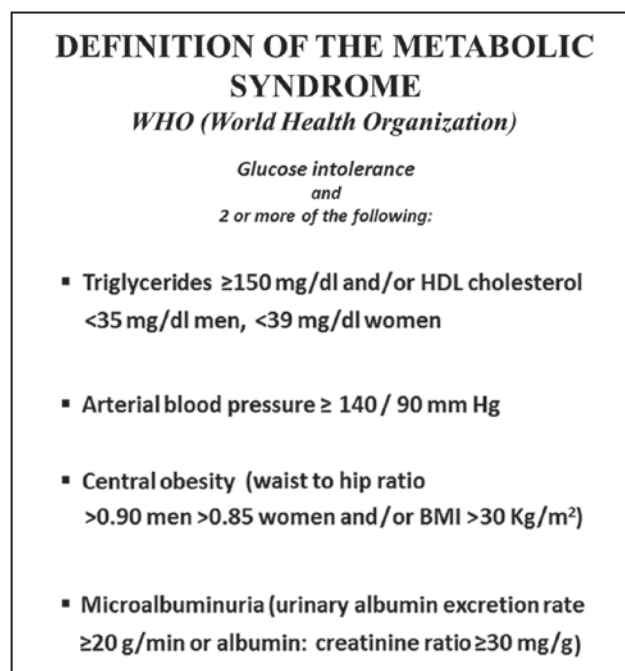


FIGURE 4. Definition of the metabolic syndrome according to the International Diabetes Federation (IDF) criteria.

with increased production of inflammatory cytokines and pro-thrombotic factors⁹ which promote atherosclerotic plaque rupture. Finally, MS has been associated with an increased concentration of the highly atherogenic small dense LDL cholesterol particles.

The metabolic syndrome is extremely common. According to the WHO definition, 25% of the USA adult population has the syndrome while 23.9% fit the NCEP ATP III criteria.⁴⁰ The results of the INTERHEART study, a large trial conducted in 52 countries, 26% of the control group had the MS.⁴¹ Men and black individuals are at higher risk to develop the syndrome, the prevalence of which increases also with age.⁴⁰ Based on data from the National Health and Nutrition Examination Survey (NHANES) the prevalence of the MS is 6.7% in persons less than 30 years old but goes up to 40% in those older than 60 years.⁴⁰

**DIAGNOSIS - PREVENTION - TREATMENT
OF THE METABOLIC SYNDROME: THE
NURSE'S ROLE**

Given the high prevalence of the MS (approximately 47 million in the USA) and its well established relationship with the increasing incidence of diabetes mellitus, coronary artery disease and stroke, prevention, diagnosis and treatment of this poly-metabolic abnormality should become a high priority

goal. The coordinated work of various health care professionals is essential to achieve high success rates in diagnosis and treatment. Among these health providers, the nurse has a very important role given her or his close relationship with the patient and her or his holistic approach to health problems. This latter approach facilitates the implementation of the integrated type of intervention required for “reversing the tide” of this major health crisis.

NURSE'S ROLE IN THE DIAGNOSIS OF THE METABOLIC SYNDROME

To establish the diagnosis of MS is mandatory to recognize its individual components through their clinical characteristics. Obesity is the most important and also the most clinically obvious abnormality of the MS. Generalized obesity refers to increased weight in relation to an individual's height and can be determined by calculating the body mass index (BMI) defined as weight in kilograms divided by height in meters square (Kg/m²). This parameter is one of the defining criteria according to the WHO's definition of the MS. It is the nurse's responsibility to accurately measure BMI. However, central obesity defined as the excess adipose tissue residing mainly in the upper body within the abdominal region, is thought to be a better diagnostic indicator of the MS. This index can be calculated either as waist to hip circumference ratio or simply as waist circumference in centimeters. Individuals with this type of obesity even if they do not fulfill any other criteria of the MS, have a high risk to develop it in the future. Obtaining of a waist circumference measurement with use of a measuring tape, no matter what the patient's overall body habitus is, should be part of the nurse's clinical routine. These measurements must be based on standard guidelines (Table 1).⁴²

Insulin resistance along with its accompanying hyperinsulinemia is the second major pathophysiologic component of the MS. Although fasting blood glucose levels may reflect the degree of hyperinsulinemia, it should be remembered that

normal blood glucose levels (<100 mg/dl) do not exclude the existence of an insulin resistance state. Thus, even though fasting blood glucose should be measured in every patient with the clinical suspicion of MS and a history of anti-diabetic medication use should always be taken, the nurse must be aware that this information is usually not enough. Two other clinical signs suggesting hyperinsulinemia must be sought and identified. These signs are: acanthosis nigrans and hirsutism.⁴³ Acanthosis nigrans is characterized by hyperpigmentation, or velvety plaques of body folds (back of the neck, axillae, elbows, knee etc). The exact etiology of this cutaneous abnormality is unknown but is thought to be caused by hyperinsulinemia.

Hirsutism, an excessive growth of hair in locations where hair growth is atypical for women and more common for men, could be caused by insulin-mediated overstimulation of the ovaries to produce androgens. In that case, hirsutism may be part of the polycystic ovary syndrome, which is a common cause of hyperinsulinemia and is characterized also by menstrual irregularities, glucose intolerance and alopecia.

Regarding hyperlipidemia, the nurse must be aware of the lipid values considered abnormal and used as criteria for the diagnosis of the MS (triglycerides ≥150 mg/dl, HDL-cholesterol ≤40 mg/dl in men and ≤50 mg/dl in women)

Finally, regarding hypertension, although it is unclear how it is caused within the MS, we are certain that its simultaneous presence even with only one other component of the MS significantly increases cardiovascular risk. Blood pressure measurements should be part of the initial assessment of every patient with the clinical suspicion of the MS. Accurate and reproducible measurements of blood pressure are not only a medical but a nursing duty as well, and to achieve these measurements the use of standard practicing guidelines is necessary⁴⁴ (Table 2). On the other hand, the use of anti-hypertensive medications confirms the diagnosis of hypertension without any further assessment and such a history must always be obtained.

TABLE 1. Guidelines for accurate patient's waist measurement

Nursing Guidelines for Waist Measurement
First have the patient face away from you and put his hands at the top of his hip bones or iliac crests. Mark this spot on each of his hip with a felt-tip pen
Put the measuring tape around your patient at the level of the iliac crest
Make sure that the measuring tape is parallel to the floor and that it is snug but not so tight that dents the skin
Wait until the patient exhales normally, then take the measurement and record it

TABLE 2. Guidelines for accurate patient's blood pressure measurement

Nursing Guidelines for Blood Pressure Measurement
Make sure that the patient hasn't had any caffeine or tobacco in the past 30 minutes
Place the patient in a comfortable sitting or lying position for at least 5 minutes prior to blood pressure measurement
Choose an appropriate size cuff (it should cover two-thirds of the area between his axilla and elbow, and 80% of the bladder should encircle his arm
Take one reading, then another 2 minutes later. If the pressure differ by 5 mmHg or more, take additional readings at least 2 minutes apart and record the average

NURSE'S ROLE IN THE PREVENTION AND TREATMENT OF THE METABOLIC SYNDROME

The final step after identifying somebody being at risk for the development of MS, is to implement measures for preventing its full clinical expression while at a later stage in a patient who has the MS, health care providers should treat all its metabolic abnormalities. The final goal is common in both situations: cardiovascular risk reduction. At any stage, patient management requires an integrated approach with the involvement of various health care providers, i.e. physicians, nurses, dietitians, pharmacists and social workers. Among them the nurse plays a pivotal role in implementing a patient-oriented therapeutic strategy with realistic goals and expectations. Cornerstones of therapy include 1) lifestyle modifications, 2) judicious pharmacologic management, and 3) collaborative provider/patient partnership aiming at patient's active participation in the achievement of the final goal.⁴⁵

Lifestyle modification is the most important but also the most difficult to achieve and sustain. It has two basic components: dietary changes⁴⁶ and regular exercise.⁴⁷ Both diet and exercise have a beneficial effect on all the abnormalities of the MS and especially on obesity. Obese patients should be encouraged to lose weight to achieve and sustain a BMI <25 kg/m². This can be done by restricting daily caloric intake (to 1200 calories for women and 1600 calories for men), reducing saturated fat in the meals and by engaging in a regular aerobic exercise program for 30 minutes daily, 5 days a week. Beyond obesity treatment, lifestyle modifications have been proven to prevent the development of diabetes and cardiovascular disease. Moreover, its contribution to the prevention of MS in adult life by reducing the childhood obesity rates seems to be of critical importance.⁴⁸ Lifestyle modifications contribute also to the dyslipidemia and hypertension treatment. Dietary guidelines suggest: total cholesterol intake less than 200 mg/day; fat intake 25% to 35% of total calories per day; saturated fats less than 7% of total fat intake; and soluble fiber 20 to 30 grams/day. Restricting carbohydrate intake to 45% to 50% of total daily caloric requirements can also help patients achieve the goal of lowering triglyceride levels. Trans-fatty acids should be less than 2% of total calories since a higher intake has been associated with increased LDL cholesterol levels. Finally, salt intake should be restricted to 2-4 g/day⁴⁹ (Table 3). Finally, enrollment in a smoking-cessation program is essential. Nicotine is a potent vasoconstrictor and has been identified as the primary cause of heart disease.

Pharmacological therapy is required for patients who are unable to achieve target levels of metabolic and blood pressure parameters with lifestyle changes alone. For dyslipidemia treatment statins are the drugs of choice.⁵⁰ Even though they do have a major impact upon triglyceride and HDL cholesterol levels they have been shown to decrease LDL cholesterol levels substantially. Of note, high LDL cholesterol significantly increases cardiovascular risk in patients with MS and reduction

TABLE 3. Lifestyle modification guidelines for the patients with Metabolic Syndrome

Nutrient	Recommended Intake
Saturated fat	<7% of total calories
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Trans-polyunsaturated fat	<2% of total calories
Total fat	25-35% of total calories
Carbohydrate	50-60% of total calories
Proteins	~15% of total calories
Fiber	20-30 g/day
Cholesterol	<200 mg/day
Total calories	Balance energy intake and expenditure to maintain desirable body weight / prevent weight gain
Salt	2-4 g /day
Weight Loss to the Desirable Level	
Exercise	

to <70 mg/dl has been proposed for these patients. Statins can be administered concomitantly with fibric acid derivatives, nicotinic acid, bile acid sequestrants or ezetimibe to effectively reduce all lipid parameters. The statin dosage should be reduced, however, when combined with fibric acid derivatives, to avoid the potential complication of rhabdomyolysis.

Treatment of hypertension is also a very important component of the treatment strategy. All classes of antihypertensive medications can be used. However, some of those seem more appropriate for the patients with MS. For example, angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers are effective in blood pressure management without affecting carbohydrate metabolism or aggravating lipid levels. They have been found to maintain renal function and are renal protective. Moreover, studies have shown that they prevent diabetes development in 23% of the patients.⁵¹

Regarding *hyperglycemia treatment*, it has been shown that its aggressive management reduces cardiovascular risk by approximately 20%.⁵² Patients with MS are by definition insulin-resistant and may benefit from the administration of a new category of hypoglycemic agents, thiazolidinediones. These drugs, rosiglitazone and pioglitazone, are essentially insulin sensitizers since they work at the cellular level to increase insulin recognition by the receptors. Thiazolidinediones along with some older antidiabetic medications, acarbose and metformin, may also prevent the development of diabetes in patients with MS.⁵³

Complementary pharmacological and non-pharmacological measures include the administration of low-dose aspirin (81-325 mg/day) in men >45 years old and in postmenopausal

women. Folic acid and vitamin B6 decrease homocysteine levels and are also beneficial to cardiovascular health of these patients. Garlic may reduce total cholesterol by 5% to 10% in patients with moderately elevated cholesterol (around 220 mg/dl). The recommendation is to eat 7 grams of garlic (a few cloves) per day. Large doses of omega-3 fatty acids (6 grams/day) may lower total cholesterol and triglyceride levels. Fish oil supplements are acceptable, but eating fish, such as cold water salmon, daily is preferred.⁵⁴

For all the above lifestyle modifications and pharmacological interventions to have a high success rate, the patient himself has to become an active participant of his treatment plan. Several studies have clearly shown that a very low percentage of patients with MS achieve their treatment goals. In the United Kingdom Prospective Diabetes Study (UKPDS), the proportion of patients achieving the target of glycosylated hemoglobin HbA_{1c} <7% after 9 years of follow-up was low (ranging from 9 to 18% depending upon treatment group).⁵⁵ The situation is similar in the USA. The third National Health and Nutrition Examination Survey (NHANES III) showed that only half of the hypertensive and another half of the hyperlipidemic patients were well controlled. Of great concern, fewer than 3.6% of the patients with both hypertension and dyslipidemia were at both therapeutic goals.⁵⁶

This huge gap between “what we know and what we have to do” for the MS can be attributed at least partially to the following patient barriers:

- Lack of awareness and understanding of the problem
- Low level of compliance due to medication adverse effects or due to reluctance to take life-long treatment
- Lack of adherence to lifestyle modifications

Dealing with this major limitation, nursing intervention can be of great importance. Basic aspects of this type of intervention are:

- Patient education in understanding the increased cardiovascular risk associated with the MS and the contribution of the various treatment modalities in risk reduction.
- Psychosocial support of the patient encouraging compliance with diet changes, with increased physical activity and with any other risk factor modifications
- Support of the patient's family, encouraging their active involvement in the implementation of a successful treatment strategy
- Involvement of the patient in his care (self-monitoring, tailoring doses based on a treatment schedule)
- Participation along with the medical personnel in the long-term follow-up of the patient, recording his compliance and assessing treatment efficacy.⁵⁷

CONCLUSIONS

Metabolic Syndrome is a particularly common clinical

entity characterized by a constellation of various risk factors associated with the development of type 2 diabetes mellitus and cardiovascular disease. Its hallmarks are dysglycemia, hypertension, atherogenic dyslipidemia and central obesity. Because MS is a constellation of disease processes, treating it requires an integrated approach with the involvement of various health care providers. Among them, the nurse can play a role of vital significance by actively participating a) in the identification of patients with MS and of individuals who are at risk to develop it and b) preventing the development of the syndrome and its cardiovascular sequelae through the implementation of a treatment plan featuring an integrated problem management approach. This plan should be developed along with the patient and has to be based upon patient's education, psychosocial support and close follow-up. The final goal is to assure the long-term compliance of the patients with both the proposed lifestyle changes and the medical treatment in order to achieve a significant reduction in their cardiovascular morbidity and mortality.

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