

CLINICAL AND PATHOLOGICAL SCIENCES  
REVIEW ARTICLE**Antimicrobial policy. Imperative need in view of the current increasing microbial resistance****Política antimicrobiana. Necesidad imperiosa ante la creciente resistencia microbiana actual**

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**ABSTRACT**

**Introduction:** Antimicrobials are one of the most used pharmacological groups in the clinical practice. Their relation to microbial resistance has been demonstrated. The rational use of antibiotics can be beneficial from the social and medical point of view; however, their use is not always the most correct one, which demands a systematic and special surveillance. A rational antimicrobial policy is necessary in the health care centers.

**Objective:** To review national and international consensuses and criteria on antimicrobial policy

in order to unify criteria and apply them the best way possible in health care centers.

**Material and method:** A bibliographic review on antimicrobial policy, antibiotics commission, and antibiotics policy was made through a search on different databases; some of them were: Clinical Evidence, The Cochrane Library, PUBMED, Google Scholar, MEDLINE, LIS, Scielo, Medscape, LILACS, Latindex, HINARI, MEDIGRAPHIC-NEWS, NIH Reporter and the Web sites of the PAHO/WHO.

**Development:** Concepts on different Cuban publications, international consensus, human

components, objectives, functions, resources, methods, strategies, and controls were considered.

**Conclusions:** The implementation of any therapeutic modification in the medical attention has to be analyzed correctly in all its dimensions: scientific, technological, and social ones. When the microbiological study is not possible or there is no antibiogram, the selection of the antibiotic should be made on the local epidemiological and clinical basis. The creation of an Antimicrobial

Policy with all its components, resources, and methodology is a necessary more than ever at present. It can be submitted to modifications with new evidences, but it has to be fulfilled to reduce both microbial resistance and the costs, in order to obtain better results.

**Keywords:** Antimicrobial policy, antibiotics policy, antibiotics commission, microbial resistance, health actions.

## RESUMEN

**Introducción:** Los antimicrobianos constituyen uno de los grupos farmacológicos más utilizados en la práctica clínica y está demostrada su relación con la resistencia microbiana. El uso racional de antibióticos puede producir beneficios desde el punto de vista médico y social, pero su uso en ocasiones no es el más adecuado y debe ser objeto de una vigilancia especial y sistemática. Es necesaria una política antimicrobiana coherente en las unidades de salud.

**Objetivo:** Revisar consensos y criterios nacionales e internacionales sobre política antimicrobiana para tratar de unificar criterios aplicables lo más uniforme posible en las instituciones de salud.

**Material y Método:** Se realizó una búsqueda bibliográfica en diferentes bases de datos: Clinical Evidence, The Cochrane Library, PUBMED, Google Académico, MEDLINE, LIS, Scielo, Medscape, LILACS, Latindex, HINARI, MEDIGRAPHIC-NEWS, NIH Reporter y en la web de la OPS/OMS sobre política antimicrobiana, comisión de antibióticos, política de antibióticos.

**Desarrollo:** Se consideraron conceptos de diferentes publicaciones cubanas y consensos internacionales, componentes humanos, objetivos, funciones, recursos, métodos, estrategias y control.

**Conclusiones:** Introducir cualquier modificación terapéutica en la atención médica tiene que ser correctamente valorado en todas sus dimensiones: científica, tecnológica y social. La selección del antibiótico cuando no es posible el estudio microbiológico y/o se carece de antibiograma debe ser hecha sobre las bases clínicas y epidemiológicas locales. La creación de una Política Antimicrobiana con todos sus componentes, recursos y metodología es necesaria más que nunca en estos tiempos. Puede estar sujeta a modificaciones con nuevas evidencias; pero tiene que ser cumplida para disminuir la resistencia microbiana, los costos y obtener mejores resultados.

**Palabras claves:** Política antimicrobiana, política de antibióticos, comisión de antibióticos, resistencia microbiana, acciones de salud.

## INTRODUCTION

Antimicrobials are one of the most widely used pharmacological drugs in the clinical practice both in Community Medicine and Hospital Medicine. They can cause much expense to the health care systems. Some studies have demonstrated that the percentage of hospitalized patients that use antimicrobial agents is high both in underdeveloped and developed countries, ranging from 22 to 66 %, but it can be even higher in Intensive Care Units. Their relation with microbial resistance has been demonstrated, among other reasons, for their inadequate use and especially because of the lack of evidence of the most frequent infection.<sup>1-7</sup>

The evaluation of the quality of prescription of antimicrobials allows to guide managers and professionals towards the efficient and safe use of them, which implies a knowledge about the prescription of the drug and the existence of a consensus for this prescription. The evaluation of indication-prescription constitutes the best way to measure the use of drugs, and it is the most accepted by doctors and international consensus group. On the other hand, we should point out that the unnecessary use of antimicrobials not only leads to microbial resistance, but can also have evident side effects for the patient (eradication of the normal flora, increase and selection of resistant strains, dangerous allergic reactions which many times are mortal, etc.). Also, from the socio-economic point of view, they cause high sanitary expenses. According to the World Health Organization (WHO), the inadequate prescription of antimicrobials, among other factors, has contributed to the current microbial resistance and has become one of the current biggest health problems, which is difficult

to solve for the moment and constitutes a great challenge at an international scale.<sup>9,10,11</sup>

The increase of antimicrobial resistance rates is not a recent phenomenon. The discussion about the capacity of the new antimicrobials to kill the existing microorganisms effectively, the emergent ones, and the ones which have become multi-resistant is widely analyzed at present. They will only be available for use in some years. The quality of prescription becomes crucial, and constitutes the most important action to preserve the effectiveness of antimicrobial drugs available at present. This is the reason why it is very important to establish an antimicrobial policy in each health care center, which should be able to guarantee the correct use of these drugs in order to diminish the effects of the current drug resistance.

The dilemma of the act of prescribing is difficult, even more if multiple causes such as internal, external, objective, and subjective ones, influence when taking the decision that only the ability and skill of the prescriber overcomes<sup>12</sup>; but then it is necessary to have some kind of guidance, information, protocol, and control of the fulfillment of this activity to conduct it the best way possible in each health care center.

It is extremely difficult to establish relationships among antimicrobial policies and the evolution of microbial resistance. Despite some studies referring to apparent beneficial effects of certain interventions on resistance have been published, the degree of evidence is considerable low.<sup>13</sup> In a recent review, it has been observed that less than a third of the intervention studies of antibiotics policy has an adequate methodology not only to demonstrate the effects on resistance, but also to

present a general evaluation of them. Most part of the studies are not controlled, and even if they deal with time series, less than three observations are undertaken. We should add other important problems to all this situation such as risk of participation, absence of randomization, and lack of follow-up as part of the interventions studied; the shortage of multicentric studies that allow to generalize the results or difficulties in order to know whether the effects are due to the own programs, or they are due to either personal or institutional factors. Besides, it is probable that in the evolution and dissemination of microbial resistance, the epidemiological factors (relations among populations, ecological niches, control measures, etc.), and the purely biological ones (nature of

### OBJECTIVE

The objective of this research is to review consensus and national and international criteria on antimicrobial policy in order to unify criteria to

### MATERIAL Y METHOD

In the last ten years, a bibliographic review on antimicrobial policy, antibiotics policy, and antibiotics commission was made through a search on different databases; some of them were: Clinical Evidence, The Cochrane Library, PUBMED, Google Scholar, MEDLINE, LIS, Scielo, Medscape, LILACS, Latindex, HINARI, MEDIGRAPHIC-NEWS, NIH Reporter, and the Web sites of the PAHO/ WHO. The ones which had high evidences in accordance with the criteria of Grading of Recommendations of

resistance mechanisms, possibilities of expansion of them) become more decisive in our antibiotic policies, also limited by the urgent need to use them.<sup>2-18</sup>

In Cuba, there is an Antimicrobial Policy, a Pharmaco-Therapeutic Committee, and specifically, an Antibiotics Committee in each health care center. In the recent context, it becomes imperative to join national and international consensus and positions on antimicrobial policy, its importance, components, methodology, and control activities in order to unify criteria based on consensus and apply them the most uniform way possible in the different health care centers, where these criteria apparently differ.<sup>12,14,19,20</sup>

apply them the most uniform way possible in health care centers.

Assessment Development and Evaluations (GRADE) were considered.<sup>21</sup>

*Level 1:* Data from controlled randomized clinical trials, meta-analysis, and systematic reviews.

*Level 2:* Results from cohort studies or case studies, and case controls. Considerations on professional experience and author's knowledge on the topic.

The terms antimicrobial policy, and antibiotics policy have been used interchangeably as it appears in the literature reviewed.

## DEVELOPMENT

### ***Some antecedents***

A policy for the reasonable use of antimicrobials has been implemented for more than three decades in face of the increasing microbial resistance. The resolution WHA51.<sup>17</sup> of the World Health Meeting in 1998 urged the united members to adopt measures with the aim of promoting the appropriate use and economic cost of antimicrobials; prohibiting the distribution of antimicrobials without prescription or qualified medical prescription; improving practices to prevent the spreading of infections and the extension of resistant pathogen germs; reinforcing the legislation to impede the manufacture, sale, and distribution of falsified antimicrobial drugs and the sale of antimicrobials in the drugstores where medications are sold to the population ; and reducing the use of antimicrobials in the raising of animals used in human consumption. Also, countries were encouraged to develop sustainable systems to detect resistant pathological germs, and keep a watch on the quantities and modalities of the use of antimicrobials and the effects of control measures.<sup>22</sup> As early as in 1983, an appeal was made by the WHO on this respect, that advised: You should always use an antibiotic which sensitivity to the germ causing the infection has been proven, or at least when it is hoped it could be possibly evidenced. Use, whenever possible, an antibiotic that has a narrow antimicrobial spectrum. Administer the drug selected at the dose and by the appropriate route to achieve the desired therapeutic effect. Administer the antibiotic during the shortest time possible. Use them by parenteral way, whenever possible.

Never use two antimicrobials of the same family. Prescribe a bactericidal together with a bacteriostatic. Benefit from the synergism of the drugs used. Keep in mind, the plasma proteins binding that the indicated antibiotic requires. Take advantage of the post-antibiotic effect of the drug used in the global strategy.<sup>23</sup>

In general, all the countries and regional consensus take some measures directed to implement a policy about the use of antimicrobials. They follow the advice from WHO experts concerning the existence of differences in views on expert roles, but consistent in most of the cases. Cuba has not been irrespective of the situation, and began to develop a policy in hospitals and other health care centers towards a better organization and purpose on this respect. Previously, in the 60's of the past century, some control measures of antimicrobials were already implemented. It started from some basis recommended by other countries.<sup>24-27</sup>

At present, the existing microbial resistance which includes multidrug-resistant and ultra-resistant organisms, requires the improvement and a better control of the antimicrobial policies in each health care center.

### ***Antimicrobial Policy***

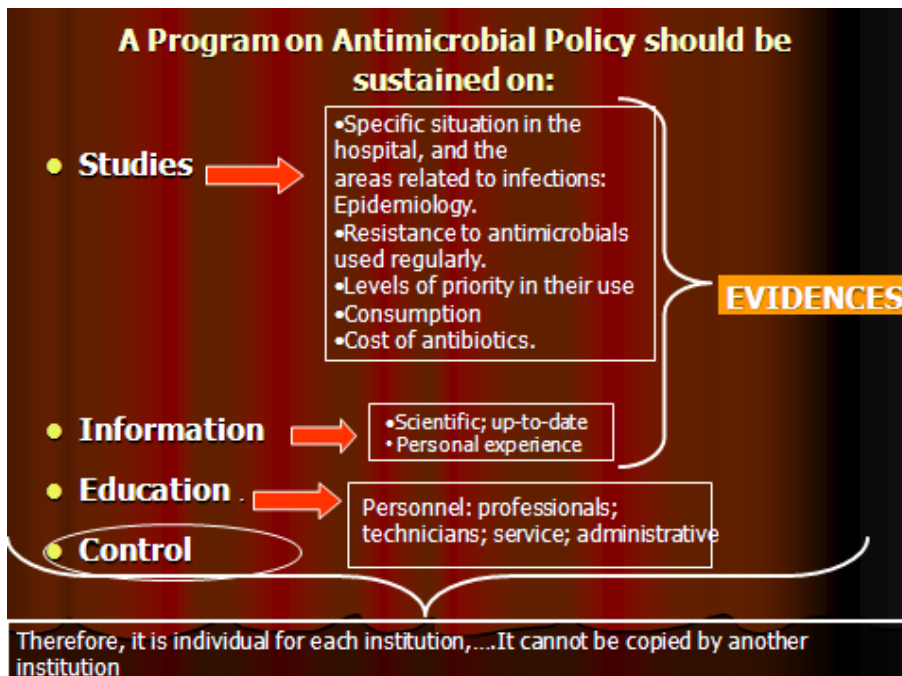
Antimicrobial Policy can be defined as: "A group of measures that have the main purpose to adapt the antimicrobial treatment for each patient in an effective way with a minimum of complications, avoid adverse reactions, control the possibility of development and the spreading of strains of resistant microorganisms, and diminish the hospital costs as much as possible". It is the set of rules that regulate the use of antibiotics in an area or sanitary center. It is a continuous process

of formulation of criteria for the adequate selection of antimicrobials.<sup>28</sup> The European Consensus about the use of antibiotics also recommends: “To control the consumption of antimicrobial agents, institute a selective list of antibiotics to be used in the therapeutic guidelines of the hospitals, and limit the introduction of all new antibiotics without certain criteria for activity, toxicity, pharmacokinetics, and costs.<sup>17,24,26</sup>

We refer to the definition of policy given by the Diccionario de la Academia de la Lengua Española: “Principles or rules that govern an activity and that are expected to be fulfilled by the employees, members of an institution, organization, party, govern, system, that leads to surveillance, regulations, controls, and measures to the offenders...” For that reason, antimicrobial policy should be sustained by a uniform methodology, as well as some components and resources that will be analyzed in more detail. A program on Antimicrobial Policy should mainly start and be sustained by Evidences. These evidences come from studies on hospital-based epidemiology conducted in each center and studies conducted in other similar centers; the determination of resistance to antimicrobials used according to the level and hospital complexity presented by the department of

Microbiology; the priority of their use; and the consumption and costs reported by the Chemist Department, taking into account the work features of different specialties. On the other hand, we have to consider the evidence of up-to-date scientific information, and personal experience of those high scientific and academic level professionals, which has been demonstrated by their performance and competence. The results of medical research are of extraordinary value as a basis for making clinical decisions. It is important to point out that most part of the decisions are empirical, but based on a reasoning and a hypothesis made by the professional, which means that it has a philosophic scientific basis.<sup>27,28</sup>

An education on this respect is extremely necessary for all the medical staff and the continuous education activities in which professionals are involved. For its effectiveness, control measures should be taken when a specific policy is carried out and established; also, it is necessary to keep in mind that these are individual programs for each institution that are subject to modifications according to new evidences. (Figure 1). Protocol and acting according clinical guidelines is very important in this stage.<sup>27,28</sup>



Considering the previous information as a starting point, we create what we call Hospital Infection Control Committee and Antibiotics Policy Committee composed of one or more representations of Clinical Services; Surgical Services; Gynecobstetric Service; Intensive Care Units; Pharmacy; Microbiology; Hospital Epidemiology; and Computing; with high-ranking resources, places, and administrative services that advice and respond directly to the director of the health care center. All this group of services and resources constitutes the known Antibiotic Commission or Antibiotic Committee.<sup>27</sup>

The objectives of the Antibiotic Commission or Antibiotic Committee are to guarantee the formulation of a coherent, wide, integrated, and interdisciplinary hospital criterion directed to treat infections and stop bacterial resistance to the antimicrobials used; promote the rational and correct use of antimicrobial agents; strengthen the adequate availability of these drugs in general, and the important antimicrobial

agents in particular; create a culture that facilitates the efficient surveillance and controls the intra-hospital infections, as well as the degree of resistance to antimicrobials in all pertinent sectors; and most of all, control the ones at the highest risk. Other important objectives are to present the main guidelines for the treatment of infections in the center to the Direction of the Hospital: Protocol or Clinical Practice Guidelines; to evaluate hospital costs periodically in this sensible area; and manage the professional activity in this field throughout the hospital.<sup>17,24,27,29-34</sup>

Some of the main functions are: Scientific study of the hospital phenomenon of antimicrobial resistance. Adequate control of the antimicrobials which are used daily. Identification and preservation of strategies for antibiotic use in the institution. Maintenance of an interdisciplinary relation, with a sense of feedback, and the necessary effectiveness of a complex system, open to the continuous



improvement and the participation of the services involved.<sup>17,24,27,30-34</sup>

**Resources and Members:**<sup>17,24,27,30-34</sup>

- A place furnished for daily meetings and case discussions.

- Experts' Committee composed of a president, a secretary, and the members that represent the clinical and surgical services that report higher incidences of infections, and have more experience to fight against them (they should be selected considering their scientific and academic level, and the accumulated fruitful work experience). Microbiology, Hospital Epidemiology, and Pharmacy. If possible, there should be a Master in Infectious Diseases or Infectiology.

- Each session should be chaired by an expert who supervises, give advice, and comments on the developmental and periodical follow-up of the patients who are registered in the database of the hospital.

- A pharmacist should be present daily to offer the control and reliability of the selected antimicrobial, which should comply with the indication and use on the same day.

**Methodology of the Hospital Infection Committee and Antibiotics Policy.**

All the system should be interrelated through the Hospital Intranet, being the following services the more important and useful: Admission and Statistics, Microbiology, Epidemiology, and Hospital Pharmacy. A weekly report on the existence of antibiotics in the hospital should be made, as well as an estimate of the ones that will be needed during the period under analysis to facilitate the pertinent management, and if necessary, with the direction of the hospital and the different authorities of the Ministry of Public

Health (MINSAP). A monthly evaluation meeting of the analysis and control of the work of all the system should be carried out. The following factors that take part in the process should be taken into account: antimicrobial use, evaluation of the microbiological spectrum of the hospital, study of monthly microbiological reports, and discussion of the data reported by the Department of Hospital Epidemiology. Reports on the controls in the weekly Word Rounds are also important, as well as the drawing up of a monthly report to the Organizational Quality Unit, in which the most relevant aspects should be mentioned.<sup>17,24,27,30-34</sup>

The policy of antibiotics should be based on criteria that are easy to observe, and modify (it should be neither strict nor static). These are: acquired scientific experience (cumulative, but changeable), that should be modified together with the progression of the most recent scientific knowledge, 28 that offers the availability of the acquisition of new drugs, allows the follow-up and control of prescription habits and patterns and adequate pharmaceutical service, and avoids the appearance of undesired side effects.<sup>17,24,27,29,30-34</sup>

There are special therapeutic problems in the prescription that should be taken into account: impairment of liver function (some antimicrobials are metabolized in the liver and excreted via the biliary route, and others have hepatotoxic effects); impairment of renal function ( a great number of antimicrobials or their metabolic products are eliminated through the kidney, others are nephrotoxic, and cause a greater damage to the renal function); alterations of the distribution volume (determined by alterations of the vascular permeability, the decrease of



oncotic pressure of plasmatic proteins, hypermetabolic state, and alterations of the cardiac output). It is also important to remember that fever does not always indicate an infectious process, and that the clinical picture should correspond with an infection. Generally, the temperatures ranging from 38.9 and 41.1 °C have an infectious origin, but the ones lower than 38.9 °C can have either an infectious origin or not, and the temperatures over 41.1 °C rarely have an infectious origin.<sup>30-35</sup>

### ***Importance of Pharmacy in Antimicrobial Policy***<sup>14,28,36,37,38</sup>

Hospital pharmacy is an administrative and clinical hospital support unit which should participate in control activities of hospital infections because it is directly related to the quality of services the health care center offers to the institution which it is part of. However, it contributes more effectively if it takes into account professional pharmaceutical products.

No matter whether he is member or consultant, the pharmacist plays an important role in the Antibiotic Commission. This way, this professional contributes to the reduction of the incidence of hospital infections, the rational and adequate use of antimicrobial therapy, and the reduction of hospital costs resulting from the use of these drugs. The pharmacist should participate in the development of regulations and procedures relative to cleaning, disinfection, sterilization, and asepsis; regulate the microbiological integrity of all products distributed by the drugstore, especially those that should be sterile; make the control card for the use of antimicrobials; conduct pharmacovigilance studies; participate in the development of protocols for the use of

antimicrobials, mainly the ones that have a prophylactic use; inform about the use of antimicrobials and their resistance indicators; provide up-to-date pharmacological information about the products in a way that it contributes with the decisions of the Pharmacotherapeutic Committee; carry out the quality control of the use of antimicrobials in the institution, which should be based on the analysis of the indiscriminate use of certain antimicrobials, the violation of the basic infection control rules, the analysis of the most frequent germs, and the use of antimicrobials in the geriatric population starting threshold in diminished immunological defenses and diminished renal excretion, and in other non - geriatric patients that suffer from immunosuppressive diseases. However, it is necessary to have a constant up-to-date knowledge to adequately fulfill these rules and functions.

It is important to remember that most of these intrahospital infections (IHI) are endemic and spread continuously, they occur more frequently in the services given to the critically ill patients, although no hospital area is exempted from it.<sup>14</sup> Unlike epidemiological outbreaks, in which the measures should be adopted rapidly in endemic infections, it is required to implement measures of a diverse degree of complexity in a coordinated form, but it demands time, organization, resources, and an Antibiotic Commission composed of a professional personnel with a high scientific and academic level.<sup>28</sup>

The pharmacy professional as an expert, consultant, and member of the Antibiotic Committee and the Pharmacotherapeutic Committee, together with the head of the pharmacy service and the rest of the members of

the Antibiotic Committee should categorize the antimicrobials. For all this, their participation should be based on the individual and collective experience, economic indicators, efficiency indicators, and the results of susceptibility studies (microbiological maps). This way, antimicrobials are divided into 3 groups: Non-controlled (group I), semi-controlled (group II), and controlled or strategic reserve (group III).

The non-controlled antimicrobials could be prescribed by all doctors from the health care center. The semi-controlled could be prescribed by the head of the services, wards, or doctors who work as teachers. The group of the controlled or reserve ones could only be authorized by the members of the Experts Committee. The head of the doctors on duty could use all of them because of the character of Emergency Medicine. If group III antimicrobials are used, the drugstore will inform directly to the Experts Committee, and the case will be evaluated to continue the treatment whether approved or not. The Experts Committee is allowed to avoid the use of some antibiotics or restrict those ones that present a high level of resistance and have become ineffective drugs.<sup>2,7,12,14,27,30</sup>

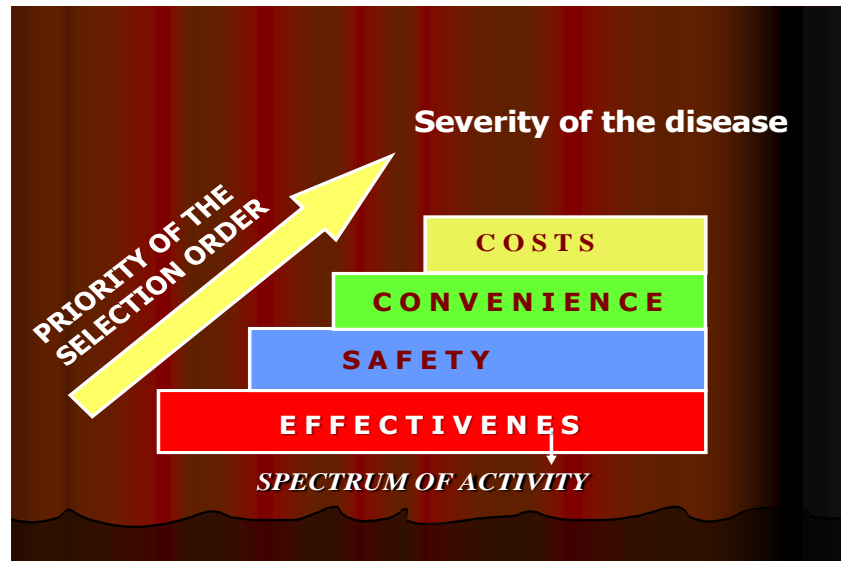
#### ***Economic issues regarding antibiotic policy***

The reduction of the use of antimicrobials and the quality of the medical attention is in relation to the Guidelines of the Social and Economic Policy that emerged from the 6th Congress of the Communist Party of Cuba, which, in Chapter 6 about Social Policy (Public Health – guideline 154)

highlights the need to “increase the quality of the service offered to the population, and the satisfaction of all the people ... guarantee the efficient use of resources, saving, and elimination of unnecessary expenses”. The last aspect shows the intention of the socialist state to promote the implementation of the scientific and technical advances in order to safeguard the health of the population with the greatest possible efficiency.<sup>39</sup> The method used for the control should not violate the principle of not affecting the patient’s therapy; should be designed in such a way that it should be administered in the correct form, moment, and way required, keeping a watch over the fulfillment of what has been established. These principles are very clear in the resolution 60/2011 of the General Treasury Inspector’s Office which establishes that its main objective “is based on a professional criterion when comparing quantitative and qualitative results with parameters and established rules” and defines the functions as the ones which “guarantee the control and supervision of the processes, activities, and operations in such a way that avoid the risk of their implementation and compensation, and limit their review or change”<sup>40</sup>

In the Instruction 206 of the Vice- Minister of Economy and the Drugs Program, The Cuban Ministry of Public Health ratifies the check and final destiny of drugs.<sup>41,42</sup>

We could summarize the main basis of the policy about the use of antibiotics in the following chart. (figure 2).



### **Limitations on the present article**

There are few publications that show high scientific evidence on this topic. It is relevant that there is a great number of descriptive investigations (residents' theses, Master's Degree theses, and others) in the different levels of health attention, which only offer a

photographic view of an identified scientific problem, but some of them could not be used in the development of this work. Other publications reviewed indicate some non-uniform criteria for undertaking an antimicrobial policy both in our country and in other latitudes; but in this article we look for a uniformity of such criteria.

### **CONCLUSIONS**

The creation of an Antimicrobial Policy with all its components, capable experts, resources, and an adequate methodology designed in a multidisciplinary way is necessary more than ever at the present time. It should be controlled, and its fulfillment should be demanded. It can be subjected to temporary modifications according to the new evidences coming from studies about microbial resistance in each institution of the Committee on Hospital Infection. The introduction of a therapeutic modification in the medical attention has to be correctly assessed in all its dimensions: scientific, technological, and social ones. For all this, an adequate formation in the study of them is necessary.

The rational use of antibiotics can have some benefits from the medical and social point of view, but, occasionally, their use is not the most adequate one; that's why the antibiotic therapy should be subject to a special and systematic surveillance. When the microbiological study is not possible for the selection of the antibiotic or there is not an antibiogram, its selection should be made on local and epidemiological clinical basis, but not on international reports since susceptibility varies on time and space; then it is indispensable to count on reliable statistical and epidemiological information that allows to give an appropriate and satisfactory treatment.

The new wisely used technologies, that are at the

service of society and the human wellbeing are one of the main pillars for the satisfaction of the increasing needs in the health area. The quality of medical attention goes on the way of economic efficiency since the rational use of material,

human, and financial resources at the moment expresses a high scientific and technical qualification and work organization, which also assures a greater use of these resources for the benefit of the patient.

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