

A Large Family outbreak of Keratoconjunctivitis in General Practice: Specific Epidemiological Implications in Family Medicine

Jose Luis Turabian*

Specialist in Family and Community Medicine Health Center “Santa Maria de Benquerencia” Regional Health Service of Castillo La Mancha (SESCAM) Toledo, Spain

***Corresponding author:** José Luis Turabián, Regional Health Service of Castillo La Mancha (SESCAM). Toledo. Spain, Centro de Salud Benquerencia, Gadarrama s/n, Toledo 45313, Spain. Email: jturabianf@hotmail.com

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Abstract

Objective: Report a keratoconjunctivitis outbreak in a single family, and assess the epidemiologic role of family doctor.

Patients and Methods: A prospective cohort study of an outbreak of keratoconjunctivitis in a single large family attended in a family medicine office was done, based on the genogram. Also, a case-control study was done to identify risk factors associated with contracting conjunctivitis. The location was a family medicine office, in Toledo, Spain.

Results: We found 18 patients with keratoconjunctivitis from May 1, 2017 and June 20, 2017, and who were evaluated prospectively (10 men and 8 women ranging in age from 25 to 86 years). The primary case in the outbreak was the mother of the family, who had been visited in the hospital consultation. The Attack Rate was 53% and the Secondary Attack Rate 50%. Analyzing possible sources and pathways of the infection, the illness was clearly related only with family characteristics. In all 18 patients (100%) recalled that a family member had also had conjunctivitis during a period of 1 week before the onset of symptoms. Patients with keratoconjunctivitis were more likely than control patients to be coexisting with another case, and especially maintain a close relationship with another case. The Relative Risk was only strong in the close relationship with one case (RR = 3.2), and moderate in the presence of polypharmacy RR = 1.5.

Conclusions: This outbreak illustrates the potential for transmission of keratoconjunctivitis infection in the family. Family medicine is a major source of information about health problems and their outbreaks, and family physicians should be alert to cases of keratoconjunctivitis, and using their specific tools, cases diagnose (“Numerator”), characterize the family (Genogram, Relationships, Pathways Of Transmission), monitor the course of the disease and the outbreak (Continuous Care), and to know all the people at risk or attended (“Denominator”), to obtain epidemiological measurements -Attack rate, incidence and prevalence-, and implement measures to prevent and treat such epidemic infection.

Keywords: Cohort Studies; Continuity of Patient Care; Epidemic Keratoconjunctivitis; Epidemiology; Family Medicine; Family Members; Outbreak of Viral Conjunctivitis

Introduction

Epidemiology is the study the distribution patterns of diseases in human populations [1]. For most illnesses, in many health systems, the general practitioner is the first point of contact in the health care system and he looks after a population whose age and sex composition is known. So, family medicine is a major source of information on health problems and their variation, and has important epidemiological connotations, presenting a unique

opportunity to study outbreaks of diseases [2].

The essence of family medicine is to assist individuals in families and communities, and this implies, on the one hand a good continuity of care, and moreover a knowledge of the nature of diseases in the community. The continuity of care is considered as a defining characteristic of family medicine and primary health care [3-6].

The person is the center of interest for the family doctor; but the importance of epidemiological research at the family physician level is often forgotten. This epidemiological level today is downplayed or underestimated; however, there have been family

physician pioneers who studied the epidemiologic problems of their community with scientific rigor. Some of them have been recognized for their seminal work in the last 125 years [7-12].

The most common eye disease in the Western Hemisphere is conjunctivitis. Viral conjunctivitis is relatively common. Viruses of the adenovirus group are responsible for pharyngoconjunctival fever and epidemic keratoconjunctivitis. Epidemic KeratoConjunctivitis (EKC) is a highly contagious disease which may be transmitted in the course of an ocular examination in a physician's office. The usual etiologic agents are adenovirus types 8 and 17. The infection has an acute onset and in 3-14 days, pain, photophobia, lacrimation, and blepharospasm are predominant. As the acute follicular conjunctivitis subsides, a keratitis develops [13].

In this context, we present an example case of an outbreak of EKC in a single large family and assess the epidemiologic role of family doctor in to knowing the attack rate, patterns of transmission, control measures and prevent future outbreaks in family and community, with the aim of reflecting and conceptualizing the importance that, for epidemiological knowledge have the data provide by family medicine

Patients and Methods

A prospective cohort study of an outbreak of EKC in a large family attended a family medicine office was done, monitoring the family members who were attended in the same consultation, and obtaining the rest of the data through questioning of these patients and the review of the computerized medical records of other relatives attended by other general practitioners, and based on the genogram (Schematic Model Of The Structure And Relationships Of A Family, Which Includes The Family Structure, The Life Cycle Of That Family, And Family Relational Patterns) [14-17]. to know the individuals exposed and the pattern of transmission. The location was a family medicine office, in the Health Center Santa Maria de Benquerencia, Toledo, Spain, which has a list of 2,000 patients.

Also, a case-control study was done to identify risk factors associated with contracting EKC. The possible risk factors studied for infection among family members were: cohabiting / non-cohabiting with a patient with previous EKC, with / without close relationship with a patient with previous EKC, with / without continued relationship with a patient with previous EKC, medications, co-morbid conditions, visits to medical specialists, and use of contact lenses or glasses of the persons with / without EKC (Cases / Not Cases). No testing of conjunctival specimens for virus isolation and / or serology was performed. No ethical approval was required for the study as this was part of a normal medical service.

Results

On May 5, 2017, the patient S (Case number 2) was treated with a highly symptomatic conjunctivitis clinic. On May 10, 2017, the D and O marriage (cases 3 and 4) was treated with a conjunctivitis clinic. Patient D was sister of patient S. Preventive measures were explained. On May 22, 2017, patient J (case 14) consulted for conjunctivitis; he was brother of D. On May 25, 2017 patient Q (case 17) consulted with conjunctivitis, who was the son of the D and O marriage; when attending this case, it was thought of an epidemic outbreak in the family. Questioned the patient, Q, reported that also his brother P (case 13) had the same symptoms, and added that other family members also had the same symptoms. From there, the family members Q, S, and J were interrogated. It was an extended family, with 9 siblings (Figure 1).

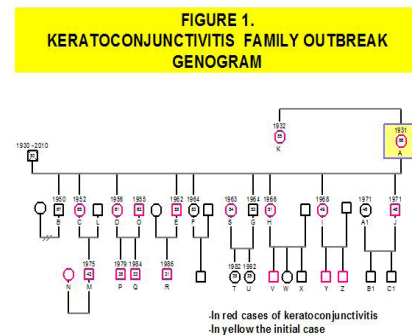


Figure 1: Keratoconjunctivitis Family Outbreak Genogram.

The next family members, D, O, Q, S, G., T, U, and J provided the rest of the data when they were questioned by family doctor. For obtain all medical data, the computerized medical records of the rest of the patients/family members were revised.

The first case occurred in the elderly mother, A (case 1), who presented the symptoms in the last days of April 2017; this 86-year-old female patient had been visited at the hospital's nephrology clinic on 18 of April 2017 (she has chronic renal failure, high blood pressure and ischemic heart disease), and presumably it was there that she contracted eye infection. This patient A, lives with her eldest son B, who is separated, but all family members rotate, according to the days, especially daughters of the extended family, as well as some of the wives of the male children, to caring to A. A sister of A, also an old woman, K, lives with A, and is equally cared for by the various members of the family. K presented EKC (case 6). C (case 5) and their children N (case 12) and M (case 10), E (case 11) and their son R (case 9), H (case 7) and their son V (case 8), and I (case 15) and their children Y (case 16) and Z (case 18), presented in this period also Patient S (case 2) was the last to heal, on June 20; Patient Q (case 17) was the penultimate cure, taking the Discharge from sick leave on June 15, 2017 (Figure 2).

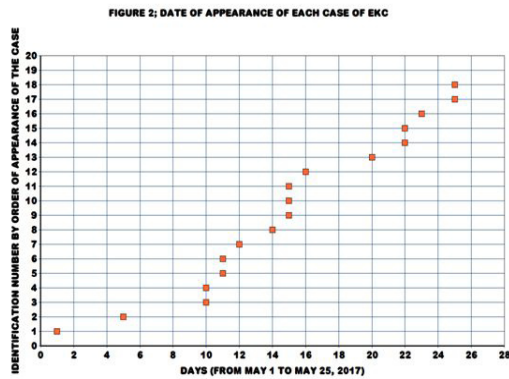


Figure 2: Date of appearance of each case of EKC.

Of the 18 cases, 8 were women (44%). The incubation time was estimated from a few days to a 2 week, and the period of transmissibility from the end of the incubation period to 15 days following the onset of the disease. (Table 1) shows the symptoms of EKC in cases.

Symptoms of Epidemic keratoconjunctivitis	Number of cases (N= 18)
Red eye	Everybody (100%)
Eyepain	
Itch	
Burning	
Photophobia	
Foreign body sensation in the eyes	
Secretions	
Blurryvision	
Cervical adenopathy	O, P, Q, and J (4/18=22%)
Follicles	S, E, I, J, D, O, and Q (7/18=39%)

Petequias	S y E (2/18=11%)
Corneal ulcer	D, O, Q (3/18=17%)
Pseudomembranes	S, D, O, Q, I, and J (6/18=33%)
Keratopathy	J, I, D, O, S, and Q (5/18=28%)

Table 1: Upper case letters identify cases (see text).

Analyzing possible sources and pathways of the infection, the illness was clearly related only with family characteristics. In all 18 patients (100%) recalled that a family member had also had conjunctivitis during a period of 1-2 week before the onset of symptoms. Family member B, who lives with A and K, however does not presented EKC; the rest of the family members explained to the family doctor that B did not actually care for A or K, but the rest of the family members, through the rotation scheme, performed this care.

Of 34 family members, 18 (Attack rate = number of new cases x 100 persons exposed = 53%; Secondary attack rate = number of new cases x 100 / persons exposed to a primary case = 50%) had onset of eye symptoms consistent with EKC between April 20 and June 15, 2017. 10 (10/34=30%) of these had onset following the onset of symptoms in a family member, despite habitual interventions and appropriate preventive measures which were prescribed, but family cases were not isolated; although the movement of relations was restricted in the family and in community, including sick leave for workers, which may have prevented an extensive viral transmission in the outbreak.

A case-control study was done to identify risk factors associated with contracting EKC. patients with conjunctivitis were more likely than control patients to be coexisting with another case, and especially maintain a close relationship with another case; these results are reasonable, because in addition to living in his family with a case, many members of the extended family maintained a relationship with the index case when taking care of her (Table 2).

	Cases (Sick) N=18	Non-Cases (Controls) (Not Sick) N=16	Statistical Significance
Living with another case	10	14	Chi-square=4.1634. p=.041306. Significant at p < .05.
Close relationship	14	16	Chi-square=9.4707. p=.002088. Significant at p < .05.
Sex woman	8	6	Chi-square=0.1687. p=.681314. Not significant at p < .05.
Age> 50 years	8	7	Chi-square=0.0017. p=.967531. Not significant at p < .05.
Polypharmacy (> 3 drugs prescribed)	5	2	Chi-square=1.2093. p=.271473. Not significant at p < .05.
Multimorbidity (> 3diseases)	9	3	Chi-square=0.5543. p=.45655. Not significant at p < .05.

Table 2: Risk Factors Associated With Ekc In Family Members.

Relative Risk (RR) was calculated as the ratio between disease rate in subjects “Closely Related to A Case of EKC”, by sex, with “Polypharmacy (> 3 Drugs Prescribed)”, with “Multimorbidity” (>3 diseases), and aged> 50 years in cases and non-cases of EKC (Table 3).

	Cases (N=18)	Non-Cases (N=16)	Rr=A/(A+B) / C/(C+D)
Closely related to a case	A=14	B=4	RR=3.2 (Strong Risk)
Not closely related to a case	C=4	D=12	
Women	A=8	B=6	RR=1.1 (Not significant risk)
Men	C=10	D=10	
Polypharmacy	A=5	B=2	RR=1.5 (Weak risk)
No polypharmacy	C=13	D=14	
Multimorbidity	A=9	B=3	RR=1.9 (Moderate risk)
No multimorbidity	C=9	D=13	
Age > 50 years	A=8	B=7	RR=0.9 Not significant risk)
Age <50 years	C=10	D=9	

Table 3: Relative Risk (Rr) [$Rr = A / (A + B) / C / (C + D)$] Of Some Selected Variables in The Cases And Non-Cases Of Ekc Family Outbreak.

The RR informs us about the strength of the association between factor exposure and disease (EKC) -the number of times it is more likely that subjects exposed to that factor become ill, relative to the unexposed. The RR was only strong in the close relationship with one case (RR = 3.2), and moderate in the presence of polypharmacy RR = 1.5.

Although testing of conjunctival specimens for virus isolation and / or serology were not performed, but an adenovirus could be presumed to be the etiologic agent.

Discussion

Viral conjunctivitis and EKC

The blink reflex protects the eye well against many potential injuries but cannot guard the conjunctivae against atmospheric influences, nor against the entry of airborne particles, some of which are inorganic dust, some are spores or pollen grains and others are airborne pathogens transmitted from one person to another [18].

Conjunctivitis is one of the most prevalent epidemic diseases in the community, and in the family environment. Viral conjunctivitis affects all age groups equally and there are frequent epidemics (widespread contagion) within the same family, school, office and organizations, and can be extended to the community from these groups. Viral conjunctivitis is usually produced by adenoviruses. The spectrum of adenovirus ocular infection varies from mild to almost non-existent to complete with significant morbidity. The two types of conjunctivitis caused by adenovirus are: 1) Pharyngoconjunctival fever, which is usually caused by adenoviruses types 3, 4, and 7 and sometimes type 5, and that is transmitted through the droplets and typically affects children who also have upper respiratory tract infection; And 2) The EKC.

EKC is an acute infectious eye disease characterized by unilateral or bilateral inflammation of the conjunctivae and eyelid edema and periorbital tissues. It suddenly begins with eye pain, photophobia, blurred vision and sometimes low fever, headache, general malaise and preauricular lymphadenopathy. Around 7 days after the onset of the disease, about half of the cases exhibit petechial haemorrhages and / or subepithelial infiltrates in the cornea. The latter can form punctiform ulcers that stain with fluorescein. Acute conjunctivitis lasts for about 2 weeks, although

keratitis may persist and leave discrete epithelial opacities that can interfere with vision. In severe cases, conjunctival membranes can be developed [19]. Thus, EKC is a combination of conjunctivitis and keratitis [20,21].

Diagnosis is confirmed by isolating the virus in appropriate tissue culture, inoculated with eye washings or conjunctival scrapings, and by increasing titre in serum neutralization tests or inhibition of haemagglutination. The infectious agent is adenovirus type 8, sometimes other types, especially 11, 19, and 29 [19,22,23]. The reservoir is man, and the mode of transmission is by direct contact with the ocular secretions of an infected person or indirectly with contaminated instruments or solutions. Outbreaks originating from ophthalmological clinics or medical offices have long been described [24]. The spread of EKC in the family is common. Immunity is usually complete following an adenovirus 8 infection; with other adenoviruses, similar conjunctivitis may occur with minor keratitis [19].

In our study, although testing for conjunctival specimens for virus isolation and / or serology was not performed, because of the symptoms of our patients, an adenovirus could be presumed to be the etiologic agent, and all EKC characteristics recur in the family outbreak presented (Table 1, Figure 1). It is accepted that the incubation period is probably 5-12 days [19], but has been reported from 3 to 22 days [20,23,25,28]. We found an incubation time that was estimated from a few days to 2 weeks, similar to what was reported.

It has been reported in outbreak of EKC due to adenovirus type 37, in a chronic care facility, an attack rate 49% [29], a figure similar to that found by us. In our study, the secondary household attack rate was 50%, higher than other reported (20%) [30].

Our initial case (patient A) had been in a nephrology consultation in the hospital in the 2 weeks prior to beginning their symptoms, so we thought that the primary mode of spread was nosocomial by contamination of the examiner's fingers, and in the family epidemic the mode of spread was close personal contact [30]. It has been reported that 30% of patients with EKC had been visited in an ophthalmology office during a period of 2 weeks before the onset of symptoms [20,26]. The reported data from outbreaks illustrate the highly contagious nature of adenovirus infec-

tion and the potential for transmission during routine office visits [23,27,28].

The relationship between the task of family medicine and the epidemiological knowledge of the outbreaks of diseases

The family doctor occupies a relevant place in the health care of the population, its role as health guardian, implies a performance fundamentally directed to the observation and action on any phenomenon or event that undermines the welfare of the community. The family doctor is the first element or fundamental component of an epidemiological surveillance system, and can be located within the clinical diagnosis subsystem, which is made up of the network of primary and secondary health care services, outpatient consultations and emergencies[31].

Family medicine is in an ideal position to conduct inquiries about outbreaks of diseases. The continuity of care is considered as a defining characteristic of family medicine and primary health care [3-6].The characteristics of family medicine imply:

- A great accessibility of patients to their family doctor, and their role of first contact with the patient: It allowing the estimation of the probability of health problems of the population (Diagnoses: Clinical Onset, Symptoms). From the epidemiological point of view, it is the access to the “Numerator”.
- Working with a population as a “Denominator”: many health problems can only be identified within a population as a “Denominator” (Attack Rate, Incidence and Prevalence) [32-36].
- Family care: The family doctor knows the life cycle of individual and family. The basics concepts of life cycle suggest an underground order of lifetime, where the individual, family, or illness exists only within a context that follows a basic sequence or not deployed. The family structure is a generic concept by which we mean a pattern, design or underground structure of the life of a person / family at a given point in her life cycle. Its primary components include: occupation, relationships, marriage, family, and roles in different social contexts[37].

The experience that the family doctor must obtain from the

family life cycle is not simply referred to an individual member of the family, but in relation to the set of demands of other members and from the external environment. The knowledge of family life cycle allows us to understand: 1.-How in the stages of transition increases the stress that can manifest as physical symptoms in some member; 2.-The strengths and weaknesses of the time that elapses the lives of the members of a family; 3.- Possibilities of the family to face difficulties; and 4.- The family as a space between society and the individual, in relation to behaviours, thoughts and feelings which are expressed from the personal and group level [38].

In our outbreak of EKC, all members of the extended family took turns, at varying degrees of time, frequency and closeness, to care for the mother (case 1) day and night, which involved different risks of contagion. On the other hand, these caregivers of the elderly mother brought the EKC to their own families. We find that the genogram is ideal document to register family structure, relationships and life cycle[14-17, 39-42].

Family physicians and other specialists working in the community, have the need to remember that the experience of the family is a crucial part of the social environment of the individual. The family provides the individual the most

Intense and influential relationships that will likely experience. However, these family relationships can mean a resource but also a problem. In addition, many problems that doctors initially identify as belonging to the individual level, may be more appropriately understood as problems of the family system. Moreover, the ill or incapacitated individual can often survive outside the institutions with the support and care provided by their families.

All this can be observed in our outbreak of EKC: the extended family means a resource for the care of the mother (case 1), but at the same time carries the risk of dissemination of the infectious disease to the whole family; Thus, an individual case must be seen within their network of relationships, and individual medical intervention becomes a family and community intervention. So, there is an area where epidemiology and family medicine are found or merged. A good starting point for epidemiological research is the critical analysis of individual patients - a man and his small world [18]. Box -1

- Detection and control of outbreaks or epidemics
- Detection of new or unknown, unexpected events, anticipating emerging situations
- Determination of the natural cause of the disease: to evaluate the incidence, geographical and seasonal prevalence of the diseases
- Evaluation of control measures
- Detection and monitoring of changes and future trends of pathogens

- A.-Preventive measures:**
- 1) Do not share eye medications; replace multidose drops by single dose
 - 2) Education about personal hygiene and the danger of sharing towels and toiletries
- B.-Patient, contact and environmental control:**
- 1) Isolation during the acute phase of the disease
 - 2) Concurrent disinfection of ocular and nasal secretions and objects contaminated by them
 - 3) Investigation of contacts and source of infection, to prevent the spread of transmission

Box 2: Methods of Epidemiological Control Applied to EKC In Family Medicine.

the methods of epidemiological control applied to EKC in family medicine. This leads to the conceptualization and systematization of a series of specific epidemiological implications of family medicine in the study of outbreaks of diseases (Table 4).

Tasks of The Family Doctor	Concept	Epidemiological Instrument	Instrument In Family Medicine
Case Definition	List of specific criteria used to decide whether or not a person has the disease or event of interest	Case index: the case that introduces the infection in the population Primary cases: people who were initially infected from the same source Secondary cases: people who become infected by person-to-person transmission from primary, often family cases	Numerator: Clinical interview, diagnosis, continued care, medical history
Outbreak Investigation and Outbreak Epidemiological Description	An outbreak or epidemic is called the occurrence of a number of cases of a disease or specific damage greater than expected in a given area within a set period of time	Attack rate = Number of new cases x 100 exposed people Secondary attack rate = Number of new cases x 100 persons exposed to a primary case	Numerator and denominator; the Importance of family characterization tools such as genograms (the importance of knowing the family)
Raise Hypotheses and Evaluate Hypotheses	a. Additional epidemiological studies	-Case-control studies to identify risk factors associated with contracting diseases	Clinical interview, diagnosis, continued care, clinical history. Genogram, population served
	b. Other laboratory and / or environmental studies	-Relative Risk (RR): the ratio between disease rate in exposed and unexposed. The RR informs us about the strength of the association between factor exposure and disease -the number of times it is more likely that subjects are exposed to that factor become ill, relative to the unexposed	
Develop Prevention and Case Control Measures	-Preventive measures -Control of the patient, the contacts and the environment -Investigation of the source of infection, to avoid spreading the transmission	Epidemiological surveillance: -Detection and control of outbreaks or epidemics -Detection of new or unknown, unexpected events -Evaluate the incidence, geographical and seasonal prevalence of diseases -Evaluation of control measures -Detection and monitoring of changes and future trends of pathogens	-Clinical interview, diagnosis, continued care, clinical history -The importance of knowing the family for prevention -The Importance of Labor-Economic and School Implications

Table 4: Specific Role and Tools of The Family Physician In The Study And Control Of Epidemic Outbreaks.

So, family medicine presents a unique opportunity to study the outbreaks of disease (Figure 3).

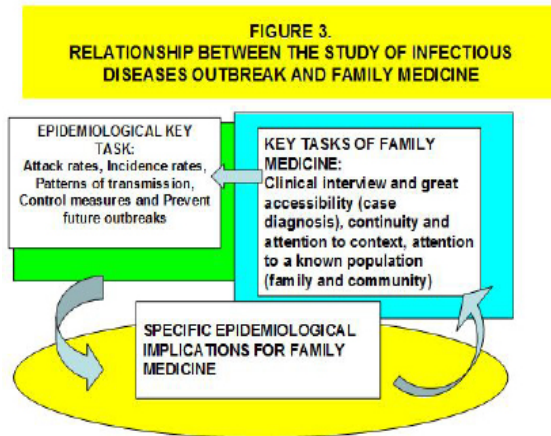


Figure 3: Relationship between the study of infectious diseases outbreak and family medicine.

Conclusion

This outbreak illustrates the potential for transmission of adenovirus infection during the provision of eye care. Family physicians should be alert to cases of conjunctivitis, and using their specific tools, diagnose (“Numerator”), characterize the family (Genogram, Relationships, Pathways Of Transmission), monitor the course of the disease and the outbreak (continuous care), and to know all the people at risk or attended (“Denominator”), to obtain epidemiological measurements, and implement measures to prevent such infection, which may prevent extensive viral transmission in the outbreak.

This study has a number of implications for household / family contacts of EKC, including the potential to reduce the diagnostic delay for subsequent household cases and the benefit of using certain tools specific to family medicine, such as clinical interview for diagnosis, the genogram for family care, and continued care to identify the source of contact, tracing the pathways of transmission outside and inside the household.

The first priority in the treatment of patients with definite or suspected EKC is the rigorous application of hygienic measures, particularly because there is still no effective drug treatment for this disease, and here the role of the family doctor to interrupt family and community dissemination, as well as in medical facilities, is a key factor.

Family medicine is a major source of information about health problems and their outbreaks. For most illnesses the general practitioner is the first point of contact in the health care system, he looks after a population whose age and sex composition is known, and he take care of the whole family and known their relationships.

The ordinary general practitioners can make a significant contribution to research in outbreaks of diseases on the basis of patients seen in routine practice.

Family medicine presents the unique opportunity to detect new cases of illness and study its natural history, since it contemplates the family life cycle continuously. The family doctor is an “Opportunistic Epidemiologist” or, in other words, “A Fisherman with Hook, Instead of With Net” (as the formal specialist in epidemiology does): he uses traditional small-scale techniques -”The Hook”- instead of “Mass Fishing Or Industrial Fishing” [43]. For the sound practice of family medicine not only traditional diagnostic and treatment skills are needed, but also the application of the understanding of the frequency and distribution of the disease in the family and community [44].

Future epidemiological strategies that use family medicine instruments as “Continuing Care”, “Family Care and Genograms”, Using Homogeneous Definitions Of Diseases, And Working With A Population As A “Denominator” should be enhanced in order to provide a basis for the development of health strategies, prevention and treatment measures in outbreaks.

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