Contact Dermatitis in a Rapidly Changing Society: Experiences in Korea

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14.1 Introduction

Contact dermatitis is closely related to environmental conditions and social status. Patch test remains essential in identifying causative materials producing contact dermatitis. However, patch test does suffer from limitations that can impede the final interpretation of the results and subsequent recommendations for patients regarding avoidance of causative agents, particularly in developing countries.

About a year ago, there was an article in an issue of Time magazine. This article claimed that since 1950 only Korea and Taiwan have maintained an average annual GDP growth rate of 5 % or more over the past 50 years, although six countries have maintained this rate of growth for four decades [1]. This suggests to us that contact dermatitis in Korea could be a good model for a rapidly changing society in a relatively short time.

This article addresses the difficulties and limitations of performing patch test in a developing country showing various experiences in Korea.

14.2 Limits of Patch Test

In principle, patch test is very simple. However, various factors can diminish the value of the final test results, which can be stressful to the performers. In countries where information gathering and patients' referral system are relatively good for the dermatologists, patch test can be attractive. However, in many countries the situation is the opposite, because of the following factors, which I would like to mention in detail.

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14.2.1 Reproducibility

Patch test is an in vivo test. Therefore, many unknown factors may affect the final patch test result. The possible factors related to the false-positive and false-negative reactions of patch test were already well described about 40 years ago by Sultzburger [2]. Compared to the time of his report, standardization of test methods has improved quite a bit. Despite this improvement, poor reproducibility of patch test remains a serious problem, which was shown well by Gaullhausen et al. [3]. In the report, if we perform the same test on the same individuals using the Finn Chambers system, nearly 40 % of the positive results were not reproducible at the sequential testing, and 43.8 % were nonreproducible at concomitant testing. The author also pointed out that weakly positive reactions are far more often nonreproducible than stronger reactions [3]. Even if using TRUE test, the most up-to-date system of patch test, 17.9 % of tests results are not reproducible [4]. This means that from the applying antigens to the final reading of the test results, many delicate factors may be involved. Therefore, the true meaning of patch test reactions needs cautious interpretation.

Patch testing is not usually recommended in patients with active skin lesions because of the possibility of false-positive reaction. However, for practical reasons dermatologists cannot always perform patch test in the complete absence of patients' skin lesions. It means that false-positive reaction due to the existing dermatitis can affect the patch test reaction all the time. As there is currently no other appropriate alternative diagnostic test for patients with contact dermatitis, patch test should be done carefully according to the guidelines to maximize reproducibility.

14.2.2 Antigens and Cost

Many commercial patch test antigens should be imported from other countries. This increases the cost of patch test, which can be relatively expensive. In addition to the frequently used standard antigens, other antigens that are rarely used are also required. However, the consumption rate is very low in many institutes if they do not test enormous numbers of cases annually. These rare antigens may not be stably maintained in storage considering their scant use. Therefore, a reasonable rate of use would be required in terms of the cost and the stability. Moreover, in many countries, including Korea, patients must pay a portion or the full cost of the test fee, which is another burden to the simultaneous testing of many antigens. In Korea only 30 antigens are covered by the national insurance. Testing involving more antigens is directly billed to the patients.

Additional antigens that are not commercially available can be difficult to prepare in terms of time and energy. Therefore, many dermatologists usually use the standard battery only, which is another reason that the test results are not so productive to make a final conclusion. In this sense, referral of testing to an accredited hospital that has access to numerous antigens may be desirable, although this option may not be readily available in many developing countries. For example, in Korea

hospitals competitively care for patients, with doctors paid according to the number of the patients they care for. Therefore, doctors do not want to refer patients to other hospitals for additional patch testing except in cases that might otherwise involve legal disputes.

14.2.3 Information and Medical System

Dermatologists who perform patch tests need information related to the suspected antigens or materials. However, access to information can be limited, especially in developing countries. Even in developed countries, information may be restricted due to proprietary interests of vendors. Getting information is the first step to verify the patient's problem; however, its approach is very much limited according to the social and medical system. With active use of the Internet, the capabilities of reference search and obtaining information have improved compared with the past. However, even though information and relevant additional materials are available to the dermatologists, it is a really challenging and time-consuming work to verify the final causative agents. In addition, patients may be reluctant to undergo retesting with the individual ingredients that have required considerable time and energy for preparation.

14.2.4 Relevance and Interpretation

A negative patch test can be a relief to the dermatologists, since it ends the search for a source of dermatitis. However, a positive patch test can prompt an arduous search for the source of dermatitis. Although certain semiquantitative scoring systems may be helpful for the evaluation of relevance, as Lachapelle mentioned [5], its level of application can vary considerably among dermatologists of different countries. Various factors such as good clinical data, environmental evaluation, acquiring information, and analysis are vital to increase the relevant scoring. However, these activities can be onerous for busy physicians who are not working under a specialized and well-designed system. This means that individual tracing of perfect relevance is not always satisfactory even in a developed society with more resources and facilities, which is another big challenge of performing patch test. There is no doubt that dermatologists in developing countries are much more likely to face this kind of difficulties.

14.2.5 Prognosis

After a patch test, a patient's skin trouble may not be relieved effectively, even when contact with relevant antigens or irritants is avoided. Some antigens are ubiquitous, and it may be the source of the persisting skin trouble. However patients' skin lesions sometimes persist even though complete avoidance has seemingly been

achieved. It is also well known that in contact dermatitis due to some industrial antigens, such as chrome, the prognosis is relatively poor, even after avoidance of the causative agent or a job change [6]. Sometimes complicated legal problems can appear, and the potential legal ramification can dissuade dermatologists from caring for patients with industrial-related problems.

14.3 Experiences in Korea

Despite the aforementioned negative aspects of patch testing, I would like to emphasize that dermatologists in a developing country should more actively use patch test as a means of safeguarding people from emerging and perhaps little-recognized hazardous agents. In cases in which we are searching well-known agents in a society, it may be easy to diagnose the culprits. However, unfamiliar agents producing dermatitis are very difficult to identify without painstaking hard work by the physicians.

Korea, one of the poorest countries in the world only about 50 years ago, has been transformed into a high-tech society. Therefore, it may be worthwhile to review various experiences in this country as a model of contact dermatitis in a developing society. With this in mind, some examples were introduced with a few practical and important ideas concerning patch test and contact dermatitis.

14.3.1 General Medical System in Korea

A necessary and important prelude to a discussion of contact dermatitis and patch test is an understanding of the general medical system of the country of concern, in this case Korea, since this will affect the performance of the patch test in various ways. The Korean medical insurance system was initially adopted from Japan in the late 1970s, but the major difference in Korea today is that it is totally controlled by one government institute. Every worker pays 5.3 % of their average income as an insurance fee, with half covered by employers. It is basically a partial coverage system. For example, the admission fee is covered at 80 % from insurance, while outpatient fees are covered at only 50 %. It is more favorable for children (90 % coverage) and for extremely poor persons who receive a complete deduction. The medical fee is inexpensive and under socialized control by the government. Since the fee is seldom increased, doctors must see many patients to match the revenue. Large hospitals are allowed to operate other related businesses such as funeral homes and restaurants to compensate for the financial burden. The greatly discounted medical insurance system in Korea contrasts with full-coverage systems in many western countries. One of the key factors worth mentioning in Korea is that the government has not invested much in hospital facilities except for regional public health centers whose roles include vaccination and control of venereal diseases, as two examples. Most hospital facilities are funded by private institutes or individuals. This system did work relatively well. But in a time when increasing numbers of hospitals are facing financial problems, discontent with the government's

monopoly of medical fee control is growing. And this conflict is getting worse due to the rapid increase of aging population, which is a great burden to the medical insurance system year by year.

14.3.2 Industrial Dermatology

One of the attractive points in the field of contact dermatitis is industrial dermatology. This is because every factory can be a good research model. Occupational dermatoses are frequently neglected even in a developed society because doctors, as well as workers, regard them as non-life-threatening conditions. Excluding some developed nations, the system does not favor dermatologists. As the systems of diagnosis, management, and compensation for industrial dermatology vary between different countries, the reporting systems are also different.

An annual routine special medical examination is the key system of managing industrial diseases in Korea and is performed by doctors of preventive medicine. These physicians are very wary of friction with the industrial companies who pay the examination fees and can change the institutes. Doctors involved in special examination generally lack clinical experiences of skin diseases. They do not want to change the present system that is oriented towards preventive medicine. They are very ambivalent to mass media reports of industrial diseases. Sometimes they acknowledge them when they appear in the headlines of newspapers, but they are afraid of them in many cases, especially when the report occurs in their operating zone. They are occasionally interested in skin research, which sometimes gives dermatologists the opportunity to participate in a certain project.

The Korean government does not want occupational diseases to appear as major issues on mass communication and has adopted a passive stance about compensation of occupational skin diseases. Officers in the labor department know the problem of managing the system of occupational skin diseases in general, but are passive in reformation. They are satisfied with low reports of occupational skin diseases in general.

Dermatologists in Korea are reluctant to care for occupational disease cases because of their already high workload and fear of legal disputes. Site visits, material analysis, and chemical information are usually not available. In addition, even though they spend much time in diagnosing occupational skin diseases, the effort is not rewarded with appropriate additional fees. Some dermatologists, including the author, are interested in limited research because many factories have their own peculiar research interests. However, fruitful results are relatively rare.

Although official reports of occupational skin disease are rare in Korea, a field survey will typically reveal a lot of occupational dermatoses without difficulty. In the early 1980s, the author surveyed in a certain industrial area as a member of a special medical examination team. Out of 4,325 industrial workers working in a hazardous environment, there were nearly 1.2 % cases of contact dermatitis [7]. As the system of diagnosis and management of occupational skin diseases has not changed much since then, similar findings would be anticipated today. One of the interesting points to mention is the perception that cases of industrial dermatoses

are decreasing a little bit nowadays in Korea because many small factories with hygienic problems prone to producing occupational skin diseases have already relocated to other countries, such as China and Southeast Asia.

Dermatologists and physicians interested in industrial medicine have tried several times to change the legislation related to industrial medicine. However the government has been stubborn to change. Therefore, it is our recommendation that a joint approach, with sophisticated tactics by dermatologists, may be more successful for the ideal setting of medical system or industrial medicine in a developing country, if the government is interested in new policies related to this field. It is because as long as we do not have a reasonable system effective for diagnosis of contact dermatitis, the patch test will remain far from being of practical help.

14.3.3 Organizing National Contact Dermatitis Research Group

Since the foundation of the International Contact Dermatitis Research Group, many national and international contact dermatitis research groups have been organized. Although the levels of activities are various, a national contact dermatitis research group in a developing country can achieve some positive results, which include:

- Stimulating reports important to their societies
- Stimulating joint studies about subjects peculiar to their societies
- Sharing information of the contact sources important to their societies
- Spurring improvements in the relevant legal system

The Korean Contact Dermatitis Research Group was founded in 1980. Since then, through annual meetings, many reports have been presented and some of them published mainly in domestic journals.

In 1995 the author reviewed around 200 Korean references related to epidemiology and clinical aspects of contact dermatitis published for the past 20 years [8]. Table 14.1 summarizes the findings and various aspects of contact dermatitis profiles. Reports related to medicaments were relatively common, while reports related to cosmetics and occupation were relatively scant. This suggested that it was relatively easy to get information from the pharmaceutical companies, while cosmetics at that time were not labeled and diagnosis and management of occupational

Table 14.1 Reported papers related to epidemiology and clinical aspects of contact dermatitis in Korea

Items	No. of papers
General incidence	13
Routine patch tests	13
Plants, animals	25
Occupation	33
Medicaments	53
Cosmetics	23
Metals	19
Others	15
Total	194

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dermatitis were poor. Unfortunately, the trend has persisted despite efforts of dermatologists to change the system related to patch test. At the present time, cosmetics are labeled; however, getting individual ingredients from cosmetic companies remains difficult, which hinders dermatologists from performing patch testing with individual ingredients because of the cost-effectiveness.

14.3.4 Standard Battery

The joint research of hospital prevalence data is always a useful indicator in any society, since it occupies nearly half of the causative agents showing positive patch test reactions. Table 14.2 shows the serial interval change of the most common allergens in Korea [9]. For instance, nickel sulfate continuously increased for the past 30 years, while chromate has recently decreased. Fragrance-related allergens such as fragrance mix and Balsam of Peru have shown a decreasing tendency. For some antigens, such as thimerosal and para-tertiary butylphenol formaldehyde resin, it is

Table 14.2 Comparison of common standard allergens with previous KCDRG study (%)

Allergen	KCDRG (1983–1985) *N* = 937	KCDRG (1986–1993) *N* = 2,326	Present study (2009–2010) *N* = 795
Nickel sulfate	12.9	17.9	34.1
Thimerosal	6.7	5.7	12.6
Cobalt chloride	NA	13.8	11.1
P-Phenylenediamine	7.3	3.4	8.4
P-tert Butylphenol formaldehyde resin	1.0	2.4	6.2
Potassium dichromate	11.8	11.3	5.6
Carba mix	NA	1.4	5.6
Fragrance mix	NA	12.9	5.2
Colophony	NA	3.3	4.3
Thiuram mix	3.2	2.6	3.7
Black rubber mix	2.7	1.0	3.5
Epoxy resin	1.2	2.5	3.3
Wool alcohols	3.0	3.3	2.9
Kathon CG	NA	NA	2.9
Neomycin sulfate	7.6	7.2	2.6
Balsam of Peru	7.0	4.7	2.6
Paraben mix	3.4	2.5	2.5
Formaldehyde	4.4	4.8	2.4
Quaternium 15	2.9	1.9	2.1
Caine mix	NA	NA	2.0
Ethylenediamine dihydrochloride	1.4	1.3	1.7
Mercapto mix	2.3	2,2	1.7
Mercaptobenzothiazole	NA	NA	1.5
Quinolone mix	NA	1.8	1.3

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Abbreviations: *KCDRG* Korean Contact Dermatitis Research Group, *NA* not available

very difficult to find the relevance. This type of research is most important to screen the prevalent allergens in their own society and can recruit more patients in a relatively short period of time. It is desirable to do joint research at regular intervals to find a serial change of a standard battery composed of common antigens suitable to their own societies.

Rhus is a very common antigen in many societies. However, it is not usually included in the standard battery because of its high risk of active sensitization. It was suggested that contact dermatitis due to Rhus plants seems to be decreasing owing to rapid urbanization [10]. However, in Korea systemic contact dermatitis due to Rhus ingestion is still problematic, since people are fond of eating Rhus with chicken to treat gastrointestinal disorders as well as a health food [11]. Nearly half of the patients have maculopapular drug eruption like rash; however, various rashes such as erythroderma, erythema multiforme, purpura, pustule, and wheals can appear. Considering the varieties of onset and some abnormal laboratory findings, several other mechanisms may be involved in addition to immunoallergic mechanism [11]. The main Rhus plant in Korea is *Rhus verniciflua* (Japanese lacquer tree), which is different from the species common in other societies such as poison ivy and poison sumac [12]. Cases with contact dermatitis from plants and animals are worth investigating in every country because a unique profile can be found in each society.

14.3.5 Rare Sporadic Case Reports

Rare clinical reports should not be overlooked, but rather considered as important, since they suggest that concurrent similar cases may exist in the particular societies. Even if the investigation is not perfect in a certain case, publication in relevant domestic journals should be encouraged. It is because the fully verified information can be difficult to obtain and patch testing with individual ingredients is not easy to perform in a developing country. Even if such clinical reports are not published in a domestic journal, recording such cases with abstracts is useful for the physicians. Also, it would be prudent for contact dermatitis researchers to establish an Internet presence, since this would facilitate contact with fellow researchers. There is no doubt that more sophisticated research of the same subject is needed for further information in detail.

Once someone has published a journal article, other authors will tend not to publish similar papers unless they involve many cases or a special investigation. Therefore, we should bear in mind that even one case may be important in representing a problem that is producing contact dermatitis at a certain period of time in a society.

Sometimes cases that occur in a domestic setting may have originated because of contact with dermatitis sources encountered during travel in a foreign country. Because native dermatologists are not used to this kind of problem, it is necessary to inform dermatologists worldwide of such cases, because it could be very helpful in diagnosing concurrent cases. Usually animals or plants

encountered during travel are frequent culprits of contact dermatitis. Contact dermatitis due to jellyfish in Korea that occurred during travel in Southeast Asia is a good example [13]. This kind of problem increases according to the rapid increase of domestic GDP.

14.4 International Cooperation

14.4.1 Information Search

Nowadays information related to contact dermatitis is usually searched for with the aid of a computer; however, we still need some kind of useful connection between physicians with the same interests in different countries. In addition, it is necessary for dermatologists to set up their own information systems to record and share information that is unique to their countries.

14.4.2 Allergen Bank

Rare allergens are quite problematic in preparations that dermatologists make themselves in patch test clinics. Therefore, in many clinics, patch tests are usually performed either with standard series only or with several additional special batteries that are commercially available. In 1996, Andersen proposed a new concept of allergen bank to solve this problem. Through this system, rare antigens can be supplied to the physicians by central control [14]. However, this method needs a controlling system, and it will also face problems of delivery, storage, quality control, waiting time, and cost. As many allergens are commercially available nowadays, it may be better to use commercial antigens, although these are expensive. Notwithstanding this, the allergen bank system still could be worthwhile to operate regionally if it can be supported by someone outside. However, it may still be difficult for the physicians to use the resources owing to constraints of time, cost, and delivery.

14.4.3 Cooperative Step Against Regulation

The safety of patch test antigens is another concern. Many governments, including Korea, are striving to ensure tight control of antigen quality and safety, especially new antigens. The Food and Drug Administration wants to verify the safety of patch tests by determining whether patch test antigens are drug or diagnostic agents. In either case, the safety issue is unavoidable because patch test antigens penetrate and are absorbed by the human body, leading to the small possibility of potential health hazard. This will be a great challenge in the future for performing patch tests. Therefore, a global cooperative approach between different contact dermatitis research groups will be necessary in this regard.

14.4.4 Sharing Educational Model

Dermatologists in many developing countries still lack enough experience in handling agents that cause contact dermatitis. This will be improved by communication between dermatologists in different countries interested in contact dermatitis and patch tests. Establishment of a practically effective national educational system would be valuable. In addition, benchmarking of other countries' models may be necessary.

Conclusion

This review highlights the limitations and problems of patch test and presents some experiences in Korea. The author hopes this information will be helpful for dermatologists in developing countries to set their own system that will prove useful for better diagnosis and management of contact dermatitis.

Practical Tips

- Although patch test is still essential for diagnosis and management of contact dermatitis, it has limitations and disadvantages that hinder its use.
- As patch test is closely related to and affected by the society and its medical system, many dermatologists are not so satisfied with the final test results, especially in developing countries.
- Despite negative aspects of patch testing, dermatologists in a developing country should more actively use patch test as a means of safeguarding people from emerging and perhaps little-recognized hazardous agents.
- Korea is one of the fastest growing countries in the world, and review of the past experiences related to contact dermatitis could be useful in establishing a model for a developing country.
- Several ideas worthwhile to stress were illustrated: organization of national contact dermatitis research group, regular joint research, importance of rare cases, and a few strategies of international cooperation.

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