

ORIGINAL ARTICLES

Allergy to stinging and biting insects in Queensland

Graham O Solley

ABSTRACT Over an eight and a half year period 742 patients were assessed for allergy to stinging and biting insects in Queensland; 452 (61%) had allergic reactions to honey bees, 244 (33%) to wasps, 30 (4%) to various ants, 11 (1.5%) to march flies (*Tabanus* sp.) and five to tick infestation. One hundred and fifty one patients (20%) presented with large local swelling only (RXN1), 98 (13%) with urticaria and/or facial angioedema distant from the sting site (RXN2) and 492 (66%) with subjective or objective evidence of dyspnoea or hypotension (RXN3). Allergy testing was performed with honey bee and wasp venoms by skin testing or by Radioallergosorbent testing. Fifty nine patients (30%) with RXN3 responses to wasps failed to react to either test, while this applied to only 19 (6%) of the patients with RXN3 responses to bee stings. Thus, a large number of wasp-allergic patients with RXN3 responses could not be offered immunotherapy. A similar problem exists in the lack of availability of specific reagents for ant- and tick-induced dyspnoea or hypotension. A whole-body insect extract of march fly, however, appears useful.

(Med J Aust 1990; 153: 650-654)

Allergy to stinging and biting insects is a significant cause of human morbidity. Observations in the United States have indicated that its prevalence ranges from 0.4% to 5% of the population.^{1,2} Fatal outcomes have also been recorded, with 40 deaths occurring annually in the United States,³ while in Australia the mortality rate is approximately one per year.⁴ During the period 1981-1989 the statistician's office of the Queensland Department of Health recorded one fatality in 1985 and two in 1986 from either bee or wasp stings. It is likely that mortality rates are higher, as an unknown number of deaths from stinging insect anaphylaxis may have been recorded erroneously as cardiovascular catastrophes.

Anaphylaxis may result from a variety of insects of the order Hymenoptera — honey bees, paper and mud wasps, and ants of various species — while a number of

patients has also reacted to bites from march flies and from tick infestation.

The diagnosis of anaphylaxis induced by these insects is based on the clinical features of the reaction, and confirmed by allergy testing with extracts from the specific insects. For many years, the diagnosis and treatment of stinging insect allergy employed insect whole-body extracts. However, in recent studies specific venom extract has proved to be superior for both uses, most importantly in the prevention of severe reactions to subsequent stings.^{5,6} Honey bee and wasp venom extracts are readily available in Australia for both diagnosis and treatment. Antigenic extracts for ants, march flies and ticks have been available only in whole-body preparations.

In this report clinical experience in the evaluation of patients in Queensland with adverse reactions to insect stings or bites is presented.

Methods

Patients

From December 1980 to June 1989, 742 patients presented for evaluation of adverse reactions to insect stings or bites; 507 (68%) were males. The patients ranged in age from 15 months to 77 years, with 282 (38%) being 16 years of age or under.

The severity of reaction in each patient was classified clinically as type 1 (RXN1) — large local swelling only; type 2 (RXN2) — generalised urticaria and/or facial angioedema distant from the sting site; and type 3 (RXN3) — subjective and/or objective evidence of obstruction to breathing (laryngeal and bronchial) and/or insufficiency of blood circulation.

Skin testing reagents

Venom extracts of honey bee (*Apis mellifera*), paper wasp (*Polistes* sp.) and yellow jacket (*Vespa* sp.) were supplied as lyophilised preparations by Dome/Hollister-Stier (DHS), division

of Bayer Australia, Sydney. The freeze-dried venoms were reconstituted with 5.5 mL of DHS albumin-saline (containing 0.9% sodium chloride, 0.4% phenol, and 0.03% human serum albumin). This resulted in solutions containing 100 µg/mL of venom. Dilutions were also made with the DHS albumin-saline.

Whole-body extracts of ants (greenhead [*Rhytidopenera metallica*], jumper [*Myrmecia pilosula*] and bull [*Myrmecia* spp.]), march fly and tick (*Ixodes holocyclus*) were supplied by the Commonwealth Serum Laboratories (CSL), Melbourne. Phenol (0.5% w/v) was added as a preservative. The extracts were supplied in A, B and C strengths. A strength contained 10 units (0.0003 mg nitrogen) per millilitre, B strength 100 units (0.0015 mg nitrogen) per millilitre, and C strength 1000 units (0.01 mg nitrogen) per millilitre.

In 1988 and 1989, march fly testing employed a whole-body extract of horse fly (*Tabanus* sp.) obtained from DHS. It was an aqueous extract containing 50% (v/v) glycerine and supplied in a 1:10 w/v strength. Ten-fold serial dilutions (1:10 to 1:1000) were prepared, using DHS albumin-saline as the diluent.

In-vivo testing

Skin testing was performed on the ventral surface of the forearm at least two weeks after a systemic response. Initial testing was done by the skin prick method using only one concentration, 10 µg/mL. A drop of this solution was placed on the skin surface and a 26-gauge needle was passed through the droplet gently lifting the outer layer of the epidermis. A reaction was considered positive if there developed at least a 2 mm by 2 mm wheal, greater than that (if any) caused by the diluent control test (sterile normal saline with phenol). If the skin test proved negative, testing was then performed intradermally. With an injected volume of 0.05 mL in each instance, serial 10-fold increments of venom extract ranging from 0.01 µg/mL to 1.0 µg/mL were used. A wheal of 5 mm by 5 mm or greater with surrounding flare was considered a positive result. In the instances in which whole-body extracts of ants, march fly and tick were used, intradermal testing only was performed in concentrations ranging from A to C strength solutions. From 1988, march fly testing with the DHS preparation was performed with 10-fold dilutions starting from 1:10 000.



DEPO MEDROL — INTRATHECAL AND EPIDURAL USE

DEPO-MEDROL has been used effectively in Australia for over 25 years.

The potential adverse effects of the intrathecal and epidural routes of administration of this drug have been highlighted in recent media reports.

These issues were previously raised by Upjohn in 1981 and 1984 in the *Medical Journal of Australia*, and the Company's position defined.

The position of the Department of Health on these routes of administration was clarified by their rejection of an application for epidural use of DEPO-MEDROL in 1982.

We believe that the manner of the recent publicity has caused alarm and distress to many patients and their doctors, and it is timely that Upjohn's position regarding this drug is restated.

- DEPO-MEDROL is a safe and efficacious drug for a wide variety of inflammatory conditions in accordance with the package insert.
- Intrathecal and epidural administration are not approved routes of administration.
- Serious adverse reactions have been reported with non-recommended routes of administration.
- Use of routes of administration other than stated in the text of the package insert is potentially dangerous.
- For further product details, refer to the prescribing information.

We believe and recommend that all patients faced with a medical problem should thoroughly discuss the situation with their doctor with special attention to the potential risks, benefits and limitations of the therapy in question.

The decision to use a specific treatment in a specific situation remains the prerogative of the doctor in agreement with, and after discussion with, the patient.

Dr David R Woodhouse
Medical Director
Upjohn Pty Limited

Upjohn Pty Limited 55-73 Kirby Street Rydalmere NSW 2116 Telephone (02) 638 0531

16 November 1990

S&H UPJ 347

In-vitro testing

If the skin testing proved negative or equivocal, specific IgE antibodies to bee venom and in the patients with wasp stings to paper wasp and yellow jacket venoms were determined by standardised methods with radioallergosorbent tests (RAST).⁷ RAST values of 2 or greater were considered positive. Testing was usually omitted in patients with RXN1 responses only, and also in a number of small children with mild degrees of RXN2 responses.

Results

Over an eight and a half year period 742 patients presented for evaluation of adverse reactions to insect stings (Table 1); 452 patients (61%) believed that honey bees caused the reaction, 244 (33%) identified paper wasps while 30 (4%) indicated various types of ants ("green", "bull", and "jumper" as well as unknown types). Reactions to march fly bite occurred in 11 patients, all but one of whom came from the Weipa area on Cape York Peninsula. Tick infestation reactions developed in five patients.

The majority of patients presented with

systemic reactions: 492 (66%) had subjective and/or objective evidence of respiratory or cardiovascular insufficiency while a further 98 (13%) had generalised skin eruptions. One patient developed temporary palsy of his left foot after a bee sting while another had the clinical features of serum sickness after a wasp sting.

Intracutaneous testing was the preferred method used to detect venom-specific allergic antibodies in the patients with bee and wasp stings. Table 2 indicates the results of the testing.

Positive reactions to skin testing were obtained in 312 patients with honey bee venom sensitivity and in 132 with wasp venom sensitivity. RAST evaluation detected venom-specific IgE antibodies in four additional patients considered to have allergic responses. One hundred and nine honey bee venom and 48 wasp venom sensitive patients did not undergo either form of specific testing. Almost all of these patients had RXN1 or mild RXN2 responses. The four patients with honey bee venom sensitivity and RXN3 responses in this group were all not interested in undergoing desensitisation and thus declined

testing. The sole patient with wasp venom sensitivity and an RXN3 response was seen in 1980, before wasp venom testing became available.

Fifty nine patients (30%) with wasp venom sensitivity who underwent testing failed to show a reaction, in contrast to 19 (6%) of the honey bee venom sensitive group. Furthermore, 51 of these patients had experienced life-threatening reactions from wasp stings, compared with only 10 of the patients with honey bee venom sensitivity (Table 2).

Table 3 indicates that seven of the 10 (70%) patients showing negative results to honey bee venom testing had had the allergic reaction more than two years before testing, and four of these had received whole-body extract immunotherapy. In contrast, only five of the 51 (10%) patients with negative results to wasp venom testing were in the same situation, with four of them having received previous whole-body extract immunotherapy.

TABLE 3: Analysis of patients with RXN3* responses and negative specific test results

Patient analysis	Honey bee	Wasp
Interval between RXN3 response and testing		
<2 years	3	46
>2 years	7	5
Previous whole body extract immunotherapy	4	8

*RXN3-subjective and/or objective evidence of obstruction to breathing and/or impaired blood circulation.

TABLE 1: Types of reactions to insect bites and stings

Insect	Patients	RXN1*	RXN2†	RXN3‡
Honey bee	452§	105	65	281
Wasp	244	44	24	176
Ant (green)	17	0	2	15
Ant (bull)	3	0	1	2
Ant (jumper)	3	0	2	1
Ant (unidentified)	7	1	3	3
March fly (<i>Tabanus</i> sp.)	11	1	0	10
Tick	5	0	1	4
Total	742	151	98	492

*RXN1 — large local swelling only. †RXN2 — generalised urticaria and/or facial angioedema distant from the sting site. ‡RXN3 — subjective and/or objective evidence of obstruction to breathing and/or impaired blood circulation. §One patient developed nerve palsy of the foot.

TABLE 2: Allergy testing

Skin test	Honey bee				Wasp			
	RXN1*	RXN2†	RXN3‡	Total	RXN1*	RXN2†	RXN3‡	Total
Positive								
Prick (10 µg/mL)	0	3	19	22	0	1	4	5
Intradermal								
0.01 µg/mL	6	16	132	154	0	5	73	78
0.1 µg/mL	8	14	103	125	0	6	37§	43
1.0 µg/mL	1	5	5	11	0	0	6	6
Total				312				132
Negative								
RAST negative	6	3	10	19	4	4	51	59
RAST positive	0	1	0	1	0	1	2	3
Not done								
RAST positive	2	1	8	11	0	0	2	2
Tests omitted	82	23	4	109	40	7	1	48
Total	105	66	281	452	44	24	176	244

*RXN1 — large local swelling only. †RXN2 — generalised urticaria and/or facial angioedema distant from sting site. ‡RXN3 — subjective and/or objective evidence of obstruction to breathing and/or impaired blood circulation. §One patient showed a positive skin test result to yellow jacket venom but not to wasp venom. RAST = radioallergosorbent test.

Before 1984 patients reacting to ant stings or march fly bites were tested with a whole-body extract of the particular insect. Five patients with ant stings and three patients with march fly bites were tested and all eight showed positive responses. Three patients with march fly bites underwent skin testing in 1988–1989 with the DHS extract of *Tabanus* sp. and all showed markedly positive responses.

Discussion

The diagnosis of allergy to insect stings and bites is determined by the clinical features of the reaction, the ability of the patient to identify the particular insect, and the demonstration of insect-specific IgE antibodies by skin or RAST testing.

Typically, the anaphylactic or IgE-mediated response begins almost immediately or within 30 minutes of the sting or bite. The spectrum of responses ranges

from large swellings only (some of which are non-immunological and considered to be toxic responses) to systemic events including cutaneous reactions such as pruritus, erythema, urticaria and angioedema; gastrointestinal symptoms such as nausea, vomiting, diarrhoea and incontinence; respiratory symptoms such as laryngeal oedema, wheezing, coughing and chest tightness; cardiovascular symptoms such as hypotension and tachycardia; and neurological symptoms such as blindness, lightheadedness and coma.

The offending insect may be incorrectly identified by the patient. The presence of a "stinger" at the sting site was indicative of honey bee stings. With wasp and ant stings, a paper nest or collection of ants was noted in the vicinity in virtually all cases. March fly and tick sensitive patients noted the insects *in situ*. There were very few instances in which the patient or responsible adult was not confident of the insect mediating the adverse response.

Skin testing with venom extracts has been shown to be the most sensitive method to confirm the presence of venom-specific IgE antibodies.⁸ Studies have indicated that 90% of patients with systemic or large local swellings from Hymenoptera stings will have positive skin tests to one or more of the commercially available venom extracts (honey bee, paper wasp, yellow jacket and hornet) at a concentration of 1 µg/mL or less.⁹ In patients who show equivocal responses on skin testing, RAST testing may also be done as occasionally the latter will show a positive result when the former is negative (Table 2).⁹

This study indicates that the bee venom test reagents detected venom-specific antibodies in all but 19 (6%) of those patients who were tested. On the other hand, tests with wasp and yellow jacket venom reagents gave negative results in 59 patients (30%). The majority of these patients (51; 86%) had experienced severe allergic responses. In addition, examination of the patients with negative test results revealed marked differences between the honey bee venom and wasp venom sensitive groups. It is possible that with the passage of time between the adverse response and specific venom testing some patients could undergo natural reduction of antibody levels (Table 3).

These data, therefore, suggest that the currently available bee venom extracts have a high degree of accuracy in detecting specific IgE antibodies but that

the wasp venom extracts do not. A study in the United States indicated that the *Polistes* venom extract was accurate in confirming the diagnosis of wasp sting allergy in eight of nine patients.¹⁰ It also showed there was some allergic cross-reactivity between *Polistes* and yellow jacket venoms.

Thus it would appear from our study that there are species of wasp in Queensland which are responsible for the induction of severe allergic reactions and which possess different allergens from those present in the *Polistes* sp. venom extract from the United States.

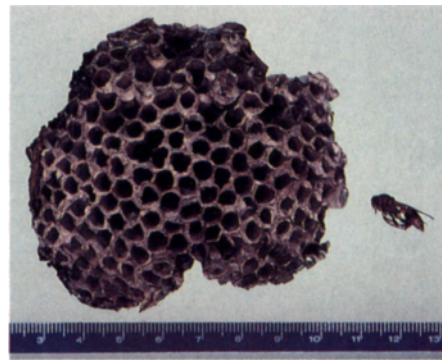


FIGURE 1: *Polistes variabilis* and nest.

There seem to be two major species of paper wasp in Queensland responsible for the severe reactions: *Polistes variabilis* and *Ropalidia* sp. The former is a little smaller than a honey bee and builds a cone-shaped paper-like nest (Figure 1). The latter is much smaller, about one-third the size, and resides in a paper-like nest consisting of two linear columns of cells (Figure 2). They are typically found in shrubs and trees, as well as on fences and even houses. Patients who test negatively for wasp venom do not seem to fall exclusively into one particular wasp sting category, that is, those patients who tested negatively were just as likely to identify the *Polistes* sp. as the *Ropalidia* sp. as the inciting agent. Similar observations appear

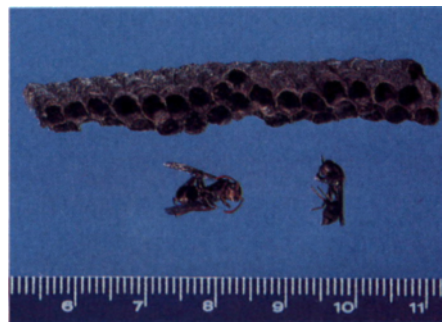


FIGURE 2: *Ropalidia* sp. and nest.

to apply to the group with positive test results.

It is of interest that a recent review of harmful Australian insects by Southcott made no reference to adverse reactions to stings from paper wasps.¹¹ It therefore appears to be a significant problem confined to Queensland and perhaps to the northern half of New South Wales.

The major indications for venom immunotherapy are a history of a systemic allergic response and a positive test result to the specific insect venom (preferably a positive skin test result rather than a positive RAST test result alone).¹² Patients who have experienced severe reactions should not receive immunotherapy if venom testing is negative. This study indicates that approximately one-third of patients with wasp stings cannot be offered immunotherapy with the currently available wasp venom extracts. As a result, venom extracts, preferably of at least one of the *Ropalidia* sp., should be made available.

A similar situation exists for patients highly allergic to ant stings. The number of patients involved in this series is smaller than the honey bee venom and wasp venom groups, although Clarke has highlighted a major problem with jumper ant stings in Tasmania.¹³ This has been confirmed in other areas of southern Australia. Severe allergy to ant stings is rarely reported outside Australia with the notable exception of allergy to the imported fire ant in the United States.¹⁴ Although fire ants have been identified here,¹¹ I am not aware of any person in Australia reacting to them. Because experience indicates that whole-body extracts of bee and wasp are much less effective than the specific venom extracts, it seems prudent that no patient newly diagnosed with severe allergy to ant stings should be treated with the currently available whole-body extracts of ant species. Rather, immunotherapy should be deferred pending the development of venom extracts of jumper and bull ants.¹⁵

The number of patients with severe systemic allergic responses to the Australian paralysis tick or scrub tick and "march" or "horse" flies is relatively small. Gauci et al. have indicated that with the former, the major allergens are found in the salivary glands,¹⁶ but production of a tick salivary gland extract is not currently feasible. A far more encouraging situation exists for patients allergic to *Tabanus*. Recent observations of three patients in this study and one from South Australia (Ann Kupa,

personal communication) indicate that the DHS preparation of *Tabanus* sp. successfully detected marked allergic skin reactivity in all four patients. Each is currently undergoing a trial of immunotherapy.

Acknowledgement

Special thanks to Dr G Monteith, Curator of Insects at the Queensland Museum, for assistance in identification of paper wasps.

References

- Settipane GA, Boyd GK. Prevalence of bee sting allergy in 4992 Boy Scouts. *Acta Allergol* 1970; 25: 286-291.
- Golden DBK, Valentine MD, Kagey-Sobotka A, et al. Prevalence of Hymenoptera venom allergy. *J Allergy Clin Immunol* 1982; 9(suppl): 124.
- Barnard JH. Studies of 400 Hymenoptera sting deaths in the United States. *J Allergy Clin Immunol* 1973; 52: 259-264.
- Harvey P, Sperber S, Kette F, et al. Bee sting mortality in Australia. *Med J Aust* 1984; 140: 209-211.
- Hunt KJ, Valentine MD, Sobotka AK, et al. A controlled trial of immunotherapy in insect sting hypersensitivity. *N Engl J Med* 1978; 229: 157-161.
- Golden DBK, Valentine MD, Kagey-Sobotka A, Lichtenstein LM. Regimens of Hymenoptera venom immunotherapy. *Ann Intern Med* 1980; 92: 620-624.
- Johansson SGO, Bennich H, Berg T. In vitro diagnosis of atopic allergy III. Quantitative estimation of circulating IgE antibodies by the radioallergosorbent test. *Int Arch Allergy* 1971; 41: 443-451.
- Hunt KJ, Valentine MD, Sobotka AK, Lichtenstein LM. Diagnosis of allergy to stinging insects by skin testing with Hymenoptera venoms. *Ann Intern Med* 1976; 85: 56-59.
- Valentine MD, Golden DBK. Diagnosis of insect sting allergy. In: Levine MI, Lockey RF, eds. *Monograph on insect allergy*. 2nd edn. Pittsburgh: Dave Lambert Associates, 1986: 57-62.
- Reisman RE, Wypych JI, Ulrich R, et al. Comparison of the allergenicity and antigenicity of *Polistes* venom and vespid venoms. *J Allergy Clin Immunol* 1982; 70: 281-287.
- Southcott RV. Some harmful Australian insects. *Med J Aust* 1988; 149: 656-662.
- Lichtenstein LM, Valentine MD, Sobotka AK. Insect allergy: the state of the art. *J Allergy Clin Immunol* 1979; 64: 5-12.
- Clarke PS. The natural history of sensitivity to jack jumper ants (Hymenoptera formicidae *Myrmecia pilosula*) in Tasmania. *Med J Aust* 1986; 145: 564-566.
- Lockey RF. Systemic reactions to stinging ants. *J Allergy Clin Immunol* 1974; 54: 132-146.
- Sutherland S. Allergy to the venom of jumper and bull ants. *Med J Aust* 1989; 150: 606.
- Gauci M, Stone BF, Thong YH. Detection in allergic individuals of IgE specific for the Australian Paralysis Tick, *Ixodes holocyclus*. *Int Arch Allergy Appl Immunol* 1988; 85: 190-193.

(Received Jul 25, 1989; accepted Aug 9, 1990)

Propolis



Propolis is a form of glue produced by bees and used inside their hives. The name comes from the Greek "pro", in front of, and "polis" meaning town or city, and bees use it to seal their hives against invasion of other insects and the weather.

Most beekeepers regard propolis as a thorough nuisance as it must regularly be cleaned from the frames and other parts of beehives and leaves sticky gum-like stains on substances in contact with it. However, in recent years propolis has been marketed as a health product and there has been a great demand for it. Beekeepers everywhere are scraping the frames of their hives and selling it for prices of up to a dollar for 10 g. It is being used as an antiseptic, as a dressing for wounds and leg ulcers, and in throat lozenges, soaps and cosmetics.

Essentially propolis is a natural resin with a pleasant aromatic smell. It varies in colour from light brown to a dark chestnut. When new, at the normal temperature of hives, it is

very sticky, below 15°C it becomes quite hard and below 5°C it is brittle. Propolis is collected by bees from the buds of trees which are coated with the brown sticky substance to protect them from moulds and infection during the months of winter and early spring. It is carried into the hives as little globules in the pollen baskets on their rear legs. A great Swiss beekeeper, Francis Huber, said in 1793 that each globule has the lustre and colour of garnet.

Propolis is usually composed of about 55% balsams and resins, 30% waxes, 10% oils and 5% pollen. The balsams and resins comprise varying amounts of many complex chemicals, and in addition to the material obtained from trees and plants, secretions from the glands of worker bees are added in the hive. The final mixture contains a fascinating variety of natural substances.

The bees use propolis to block up any opening in the hive smaller than 4.75 mm and to varnish all the inside surfaces of the hive,

not only the woodwork of the hive and the frames, but even the wax cells themselves. Inside a hive the atmosphere is warm and humid with tens of thousands of bees crowded into a small space. This provides the conditions for all kinds of bacteria and moulds to flourish. The presence of propolis varnish prevents these occurrences as it does on the buds of trees.

A mixture of beeswax and propolis is much stronger than beeswax itself and the bees use the mixture to make the combs stronger where they are attached to the wooden framework of the hive (either man made or in a hollow tree). Two thousand years ago Pliny, the Roman naturalist and observer of bees, reported such use of propolis.

When small intruders enter a beehive, for instance a wasp, they are soon destroyed and thrown out by the bees; however, when an intruder is too large to move (for example, a large moth or a mouse) bees first kill the invader then encase the carcass in propolis so that it does not rot and cause a bad smell but slowly mummifies.

Some beekeepers use propolis as a glue in wood-working, particularly when making up hives. One beekeeper reported that he kept a large lump of propolis and rubbed it all over the woodwork inside empty beehives. This technique attracted swarms of bees which were brought by the scent and it was no longer necessary for him to go out and collect swarms, as they came on their own to the baited hive.

In the past, natural balsams such as propolis were much used; for instance, maidens would tend knights wounded in battle using sweet smelling balsams. There is evidence that in prehistoric times, surgery was made possible by the use of propolis as an antiseptic. It was obtained from wild bee nests and used with honey as a dressing. As recently as the Boer War, 90 years ago, an ointment of propolis and Vaseline was used to treat battle wounds.

The greatest maker of violins in history was Stradivarius. He varnished his violins with propolis harvested by bees around Cremona in Italy. Violin makers still use propolis for the same purpose. In some countries soap and lozenges containing propolis are on sale, and with each year that remains of this century we will probably see other uses of propolis being rediscovered.

W McL Thomson
11 King Street, Sandy Bay,
Hobart, TAS 7005

Illustration reproduced with the permission of the Institute of Honeybee Science, Tamagawa University, Tokyo, Japan.