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Modified Vaccination Technique Designed to Prevent and Cure Chronic Disorders

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Abstract

In spite of enormous efforts there have been no solutions to date for preventing/terminating chronic disorders of humans by vaccination or drugs. Yet it is well understood that if the target antigen (ag) could be presented appropriately to the cells of the immune system then solutions could be found. Recently, the Barabas research group has introduced and described the third vaccination method – called modified vaccination technique (MVT) – which has the ability to provide a corrective immune response in experimental animals with an autoimmune kidney disease. Injections of immune complexes – made up of the target ag and specific non-pathogenic IgM antibodies directed against the target ag – achieved downregulation of pathogenic immune responses and tolerance to self was regained. Utilizing the immune system's natural abilities to respond to corrective information, the MVT was able to prevent an autoimmune kidney disease from occurring (prophylactic effect) in experimental animals, and when present, terminating it (therapeutic effect) specifically and without measurable side effects.

It is predicted that the application of the MVT will have the potential in the future to revolutionize the preventative and therapeutic options for dealing with chronic disorders in humans (such as autoimmune disease, cancer and chronic infections) and achieve cures.

ABBREVIATIONS

aab: Autoantibody; aag: Autoantigen; ab: Antibody; ag: Antigen; BB: Brush Border; GBM: Glomerular Basement Membrane; HN: Heymann Nephritis; IC: Immune Complex; MGN: Membranous Glomerulonephritis; MVT: Modified Vaccination Technique; rKF3: Rat Kidney Fraction 3; rarKF3: Rat Anti-Rat Kidney Fraction 3; SPHN: Slowly Progressive Heymann Nephritis

INTRODUCTION

Vaccination to prevent infectious and contagious diseases to occur in humans was first employed by Edward Jenners in 1796 to protect against small pox. He used cow-pox derived vaccinia and scratched the viral fluid on the upper outer aspect of the arm. Being an antigenically similar but not a pathogenic disease causing virus in humans, it protected the vaccinated host by developing cross-reactive antibodies (abs). After small pox vaccine, several other vaccination programs were implemented, first by Pasteur and subsequently by others. In fact, prophylactic vaccination to protect humans from several infectious and contagious diseases to occur is successfully employed today. Prophylactic vaccination works by an active immunization program. Most often an attenuated or killed bacteria or virus is introduced into the vaccinated host with or without adjuvants. The individual's immune system by responding to the injected material produces neutralizing and/or microbial killing abs which are able to eliminate the infectious agent.

The second form of vaccination is called passive immunization. It was introduced by von Behring in 1891 against diphtheria and tetanus. He produced anti-toxins in horses and rabbits against the two bacterial toxins. The injected ab in the infected host neutralized the tissue damaging toxins and the lives of most patients were spared. Since abs were produced in horses and rabbits they caused Arthus reactions, especially in tetanus treated patients, when injected with the product for the second or subsequent times. Since the employment of active immunization programs and antibiotics to protect or treat diphtheria, tetanus and numerous other bacterial and viral agent causing diseases, passive immunization is no longer widely utilized in medical

practice. However, passive immunization started to be employed quite extensively in the last few years for different treatments. Recently, monoclonal abs are produced against cancer specific antigens (ags) and cell lines to treat patients with various forms of cancer and autoimmune diseases [1-7]. The treatment programs require the injection of humanized monoclonal abs to target cell surface receptors to reduce disease causing events.

Animal experiments in mice predisposed to breast cancer using prophylactic vaccination from eight weeks of age against Alpha-lactalbumin (a cancer specific target ag which is present abundantly on breast cancer cells) revealed that a protective pathogenic autoimmune response prevented the development of breast cancer [8-10].

While both forms of vaccinations (active and passive immunizations) have useful and beneficial properties they cannot successfully terminate autoimmune disorders such as autoimmune diseases and cancer. The reasons are many:

- In autoimmune disorders, quite often the etiology and pathogenesis of the disease are not known and equally how to remove the modified autoantigen (aag) from the system which maintains the disease.
- In cancer, it is often not known how to target cancer cells, with unique cancer specific antigenic surface markers, for elimination without causing collateral damage.

The Barabas research group realized and subsequently demonstrated that special immunological interventions were needed to deal with the modified endogenous ag initiated and maintained disorders. They developed the third vaccination program that is called modified vaccination technique (MVT) [11-14]. It promises to prevent the development of certain autoimmune disorders, and when present, terminate them specifically with minimal side effects, utilizing the immune system's natural abilities to respond to corrective information present in the inoculum.

GENERAL BACKGROUND

Presently available vaccination techniques are unable to prevent or treat chronic ailments such as cancer, autoimmune diseases and chronic infections. Yet it is known for certainty that the presentation of ags to the cells of the immune system, whether exogenous or endogenous in nature, determine the immune response outcome. The same exogenous or endogenous ag that can cause disease – in our opinion and experience – can also provide cure if it is presented to the cells of the immune system in a suitable form.

While most exogenous infectious agents such as tetanus, measles, whooping cough, smallpox etc. are well represented in vaccines to evoke protective immune responses in immunized hosts, endogenous ags are not, whether present in natural forms or in purified extracts [15,16]. Induction of prophylactic and therapeutic responses to correct/terminate autoimmune diseases and cancer are complex. The purpose of this scientific paper is to describe and highlight those corrective immune responses which we have developed and could achieve – with minimal side effects – regained health. While certain environmental agents can cause or contribute to the development of the above disorders [17-26] we are mainly interested in those immunological processes which allow regained tolerance to self; tolerance to those intact healthy cells which serve special functions.

Chronic disorders caused by outside (bacteria, virus) [14] and inside agents (such as chemicals, toxins etc. making self to modified self ags) [25,27] cannot presently be prevented or treated by available medical interventions specifically without causing side effects. We still rely on experiments carried out in mice, rats etc. to study the etiology, pathogenesis [27,28] and possible treatment options [29] of chronic ailments using drugs, monoclonal abs [4,30-33], radiation, surgery etc. Yet in most instances corrective immune mediated responses – would we know how to implement them – could result in recovery [34]. Since we have worked with Heymann nephritis (HN) [35-37] and slowly progressive Heymann nephritis (SPHN) [27,38] for years, we shall illustrate and describe the various immune events in normal and in SPHN rats and how to reinstate normal health by terminating pathogenic autoimmune disease causing events [12,29].

SPHN in Wistar rats was induced by injections of chemically modified rat kidney tubular extracts in Alum [38]. Animals developed the autoimmune kidney disease slower than those which were injected with the same tubular fraction in Freund's complete adjuvant [35]. The disease was characterized by the presence of circulating pathogenic IgG autoantibodies (aabs) [36], directed against the nephritogenic ag, causing primary injury to the renal proximal convoluted tubular brush border (BB) [38] and secondary injury to the glomeruli by depositing immune complexes (ICs) [38]. The two renal injuries to the proximal renal tubular BB and the glomeruli took the following course:

- The pathogenic IgG aab, directed against the renal tubular fraction injected ag, targeted the nephritogenic ag which is abundantly present in the BB region of the renal tubules. Indirect fluorescence ab tests (using dilutions of sera on normal rat kidney sections and fluorescent labelled anti-rat IgG ab) convincingly demonstrated the intensity of the attack of the circulating ab against the renal tubules [38].
- For years it was not understood, and in the meantime was controversial, why massive deposition of ICs – made up of the nephritogenic ag and pathogenic IgG aabs directed against it – settled on the epithelial side of the glomerular basement membrane (GBM) in HN, causing membranous glomerulonephritis (MGN). It has recently been shown by Barabas and colleagues that HN susceptible strains of rats [39] have tiny depositions of ICs around their glomeruli, made up of the nephritogenic ag and non-pathogenic IgM aabs directed against them [28]. More massive deposition of the same IC can be observed in the mesangium [28]. The fact is that these rats have minimal yet significant amounts of tubular nephritogenic ag in the glomeruli. When pathogenic IgG aabs are produced, following injections of the chemically modified nephritogenic ag in Alum, they not only target the BB region of the renal proximal convoluted tubules but the glomerular localized nephritogenic ag as well; and start an ag:ab reaction on the epithelial side of the GBM leading to chronic progressive deposition of ICs in the presence of complement [38,40].

The source of the nephritogenic ag in the circulation and in the glomeruli is from the pathogenic IgG ab damaged BB region of the proximal convoluted renal tubules.

The fate of the released nephritogenic ag from the kidneys of normal and SPHN rats into the circulation is as follows:

- Most nephritogenic ag released into the circulation is removed by cross-reactive non-pathogenic IgM aabs [41-44]. ICs formed by [nephritogenic ag X non-pathogenic IgM aabs directed against the nephritogenic ag] are degraded into small molecular weight re-utilizable peptides by mononuclear cells [45-47] (Figure 1).
- Some of the nephritogenic ags will stimulate the production of specific IgM aabs. These IgM aabs being cross-reactive are protective by nature and slow down pathogenic immune events by removing both modified and released native nephritogenic ags from the circulation thereby preventing/diminishing pathogenic IgG aab production and deposition of ICs (nephritogenic ag X pathogenic IgG aabs directed against the nephritogenic ag in the presence of complement) in the glomeruli.
- Some of the released nephritogenic ag will contribute to continuous formation of ICs in the glomeruli made up of layered deposition of nephritogenic ag, IgG aabs directed against the nephritogenic ag in the presence of complement (C-3, C5b-9) [40] (Figure 2).
- For immunopathological events to continue, the presence of modified nephritogenic ag, the 'modified self,' to produce pathogenic IgG aabs is an essential requirement [27].
- In the absence of native and modified nephritogenic ags in the circulation pathogenic IgG aab production declines and eventually ceases [48].

Fate of the modified nephritogenic ag is as follows:

- The administered modified nephritogenic ag, being foreign like, will initiate and if it is continuously present in the circulation will maintain the production of cross-reactive pathogenic IgG aabs directed against the modified aag which is present in the circulation and the nephritogenic ag which is present in the BB region of the renal proximal convoluted tubules. Having direct access to the native ag, the pathogenic IgG aab will cause morphological and functional changes, e.g., in HN and SPHN, in the BB region of the renal proximal convoluted tubules (the site where nephritogenic ag is present) and in the glomeruli, where IC depositions cause proteinuria [38] [Figure 3].
- There are specific non-pathogenic IgM aabs in the circulation throughout life directed against subcellular components [49]. When cells come to the end of their life span or damaged by various outside agents (such as toxins, drugs, chemicals, infectious agents, adjuvants etc.) [17,21,27,50-54] and released into the circulation some may become modified. If the modified aag represents a relatively small amount of cellular breakdown products, then specific cross-reactive non-pathogenic IgM aabs will assist their removal, thereby preventing toxic accumulation of degraded protein and possible production of pathogenic IgG aabs. However, if the modified aag is continuously available in the system (due to modifying agents being present) then developing pathogenic cross-reactive IgG aabs could start and maintain the autoimmune disease.
- Efficient removal of both modified and native damaged and released subcellular components from the circulation by specific non-pathogenic IgM aabs and mononuclear cells could prevent the occurrence of autoimmune diseases [55-57].

Autoantigenic components and aabs playing roles in the autoimmune disease SPHN

There are two aags and two aabs present in the system during SPHN [38]. Native and modified nephritogenic aags, and specific cross-reactive IgM aabs directed against native and modified nephritogenic ags and specific cross-reactive IgG aabs directed against native and modified nephritogenic ags.

One of the aags is the native nephritogenic ag which is frequently released from the BB cells of the renal proximal convoluted tubules into the circulation and urine. This aag is responsible for the continuous production of non-pathogenic cross-reactive IgM aabs against the nephritogenic ag during health and also during disease [38]. However, a portion of the native aag in the form of ICs [native nephritogenic aag X rat anti-rat nephritogenic aag IgG aab] and [native nephritogenic aag X rat anti-rat modified nephritogenic aag IgG aab] can also produce pathogenic IgG aabs during the course of the autoimmune disease [40].

The other aag is the modified nephritogenic ag which is derived from the renal proximal convoluted tubules after being released into the circulation and modified. This ag is responsible for the production of cross-reactive pathogenic IgG aabs directed against the BB zone of cells of the renal convoluted tubules; and it is also directed against the chemically or adjuvant modified nephritogenic ag [27,51]. During SPHN both aags are targeted by the developing cross-reactive pathogenic IgG aabs contributing to renal proximal convoluted tubular and glomerular injuries and to further production of pathogenic aabs by ICs made up of the [modified nephritogenic ag X rat anti-rat modified nephritogenic ag IgG aab]. Immunopathological events will continue as long as the modified nephritogenic ag is present in the system and capable of producing pathogenic IgG aabs [40,58]. As mentioned:

- The cross-reactive pathogenic IgG aab contributes to autoimmune disease development and progression [58]; while the other
- Cross-reactive specific non-pathogenic IgM aab – directed against the nephritogenic ag – is responsible for the removal of both modified and native nephritogenic ags from the system [11,48,58]; and if the modified nephritogenic ag is diminished or becomes absent in the circulation, terminating autoimmune disease causing immunological processes, leading to full recovery.

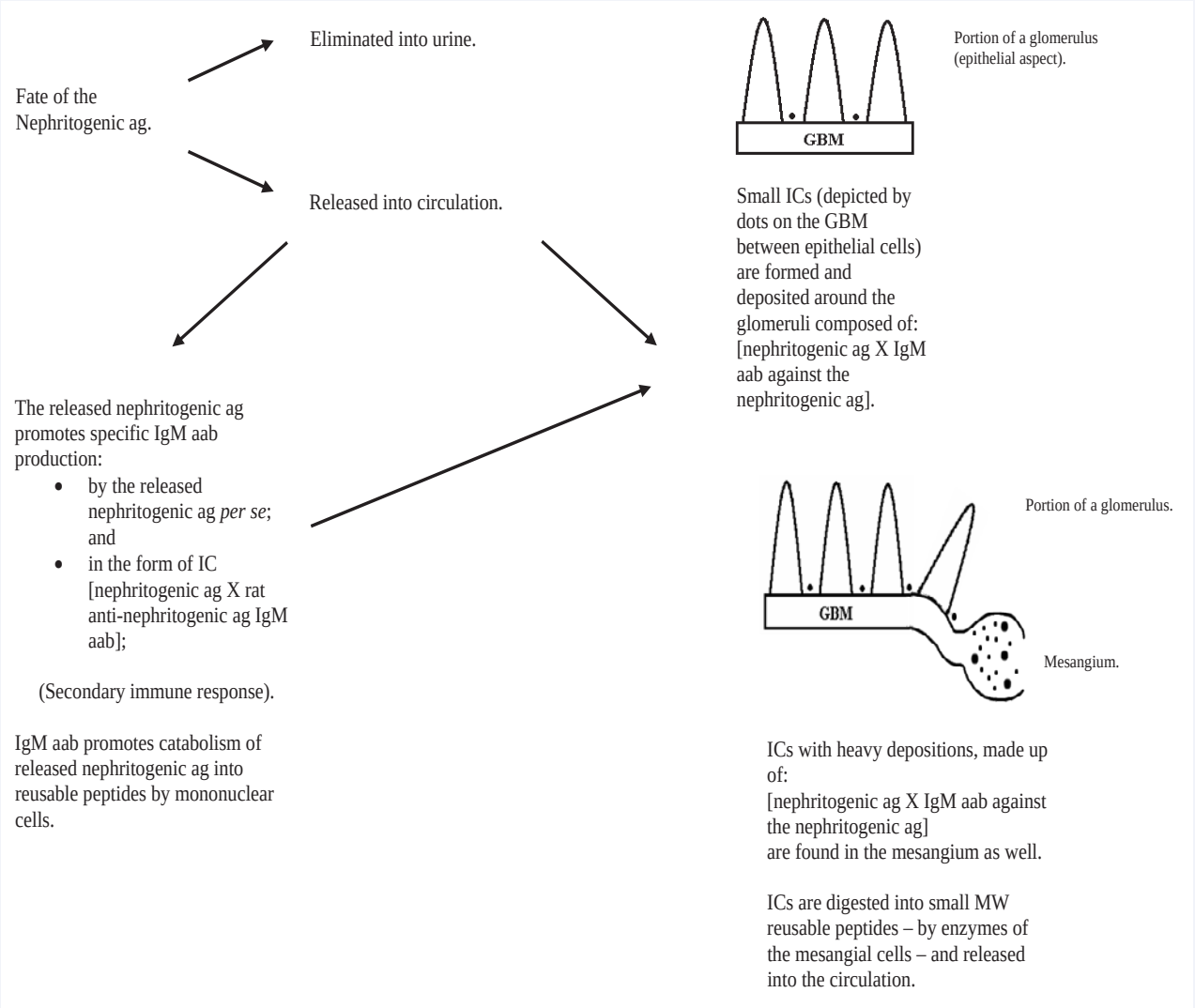

Figure 1

Title: The fate of the nephritogenic ag released from normal renal proximal convoluted tubules into the circulation. Physiologic events

Explanation: The continuously released nephritogenic ag from the renal proximal convoluted tubules promotes both the production of specific IgM aabs and its catabolism into small MW peptides by mononuclear cells.

Abbreviations: aab, autoantibody; ag, antigen; GBM, glomerular basement membrane; IC, immune complex; MW, molecular weight.

Nephritogenic aags, and aabs against the nephritogenic ag, in normal healthy, and in regained tolerance to self rats' circulation

During healthy state, only normal cellular breakdown products are present in the circulation; e.g., cell debris from the BB region of the renal proximal convoluted tubules derived from end of life span cells. These released aags initiate and maintain throughout life continuous production of specific non-pathogenic IgM aabs which assist in the removal of cellular breakdown products [41,43,46,59]. In a physiological sense there is no tolerance to inside cell located cellular components of normally functioning cells [43,44] and when cellular components are released from damaged or end of life span cells they are removed to prevent their toxic accumulation or possible modifications.

SPHN rats with regained tolerance to self from a modified nephritogenic ag caused autoimmune disease – after treatment with the MVT – have native nephritogenic ag and specific non-pathogenic IgM aabs in their circulation; the latter directed against the nephritogenic ag [60,61] just as it occurs in normal rats [11].

Lesions observed in the tubules and glomeruli of SPHN rats

The developing pathogenic IgG aabs, following injections of the modified nephritogenic ag, are directed against the injected renal tubular BB associated nephritogenic ag; and thereafter target the renal proximal convoluted tubule's BB zone of cells [40,62] (primary damage to the kidney) and by damaging them release into the circulation and urine intracytoplasmic

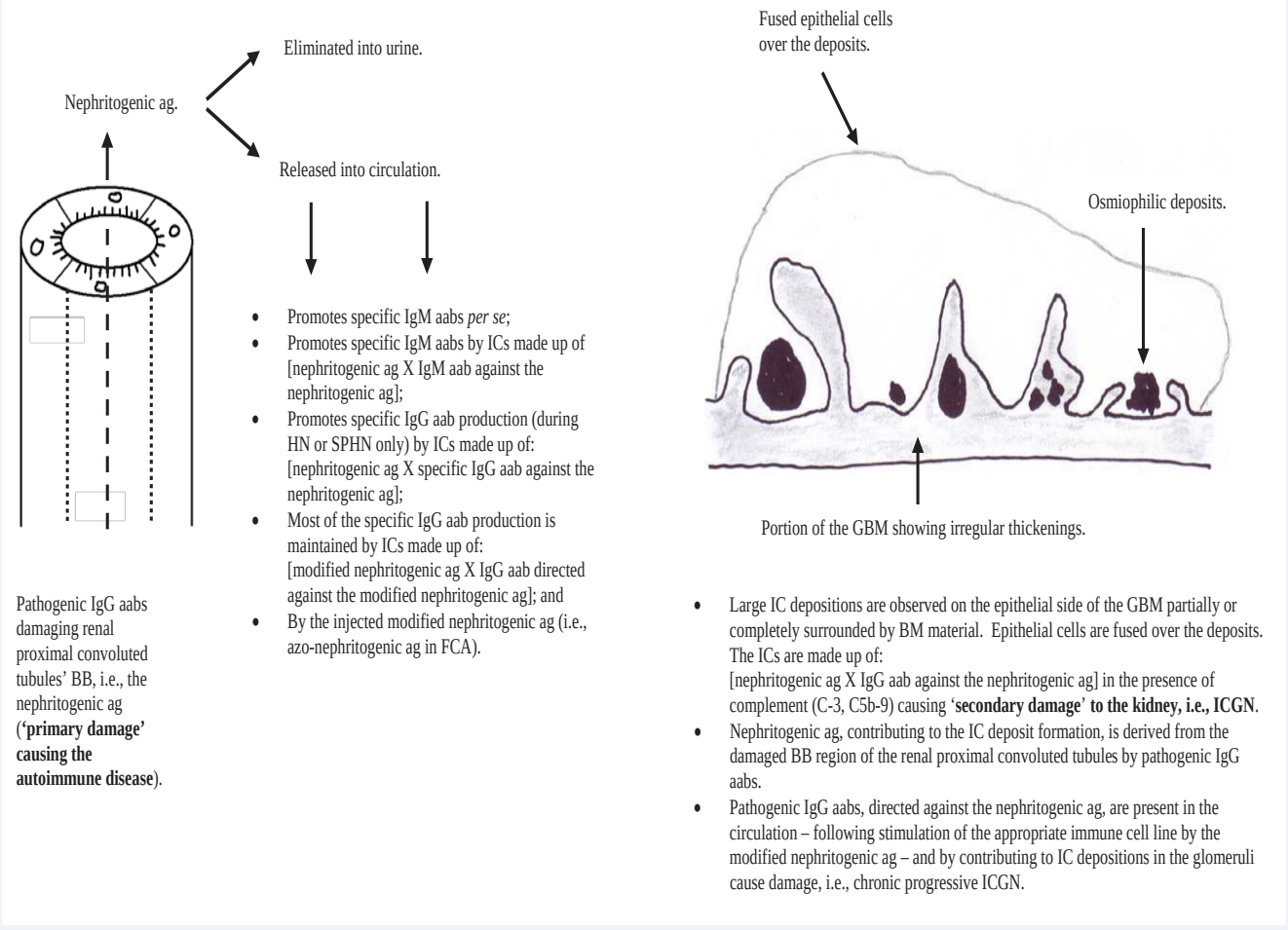

Figure 2

Title: The fate of the nephritogenic ag released from damaged renal proximal convoluted tubules into the circulation by pathogenic IgG aabs. Pathogenic events

Explanation: Nephritogenic ag is always present on the epithelial side of the GBM of genetically predisposed strain of rats as small ICs made up of: [nephritogenic ag X IgM aab against the nephritogenic ag]. Glomerular damage in HN and SPHN is possible because of the presence of the nephritogenic ag (derived from the BB region of the renal proximal convoluted tubules into the circulation) in the glomeruli which can be targeted by the developing pathogenic IgG aabs. Layered depositions of ICs in the presence of complement can occur in the glomeruli as liberated nephritogenic ag and pathogenic IgG aabs against the nephritogenic ag become available from the circulation.

Abbreviations: aab, autoantibody; ag, antigen; BB, brush border; BM, basement membrane; FCA, Freund's complete adjuvant; GBM, glomerular basement membrane; HN, Heymann nephritis; IC, immune complex; ICGN, immune complex glomerulonephritis; SPHN, slowly progressive Heymann nephritis.

components including the nephritogenic ag. Severe injury to the tubules and glomeruli results in compromised re-absorption of glomerular filtrate, including proteins by the renal proximal convoluted tubules. The most obvious lesion is found in the glomeruli (secondary damage to the kidney) where layered deposition of nephritogenic ag and pathogenic IgG aabs directed against the nephritogenic ag in the presence of complement (C-3, C5b-9) are observed on the epithelial side of the GBM. In the process of IC formation – resulting in osmiophilic deposits, as observed by electronmicroscopy – foot processes are fused and deposits are surrounded partially or completely by basement membrane material [40,63]. Changes in the GBM and epithelial cells lead to non-selective proteinuria through the irregularly thickened GBM.

The third vaccination technique for the prevention and when present termination of an experimental autoimmune kidney disease SPHN

The third vaccination method (i.e., MVT) can produce powerful predetermined immune response outcomes against both exogenous [64,65] and endogenous ags [11-13,29,48,58,66-69] without the use of adjuvants. We describe its applicability in an autoimmune kidney disease below.

In a significant way specific IgM aabs [41,43,46] – which are present in the system throughout life [43,44,70] directed against intracytoplasmic components – together with mononuclear cells [42,71] are responsible for the maintenance of tolerance to self [47]. When cells break down due to outside influences or when

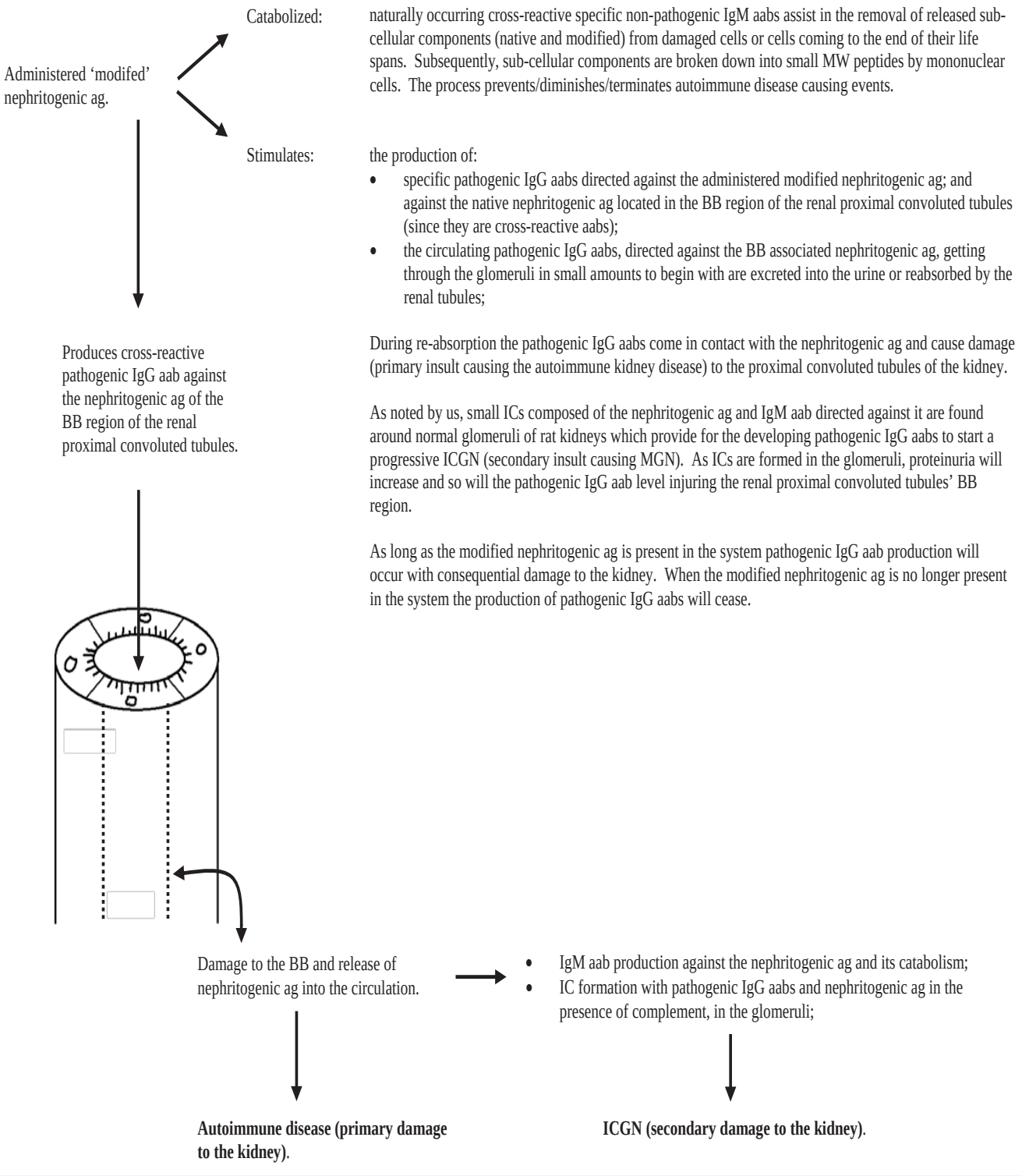

Figure 3

Title: Fate of the 'modified' nephritogenic ag administered to rats to induce SPHN. Pathogenic events.

Explanation: The injected 'modified' nephritogenic ag in the rat produces cross-reactive pathogenic IgG aab (directed against the BB region of the renal proximal convoluted tubules) and it is responsible for the development of an autoimmune kidney disease SPHN (primary injury to the kidney) and ICGN (secondary injury to the kidney).

Abbreviations: aab, autoantibody; ag, antigen; BB, brush border; IC, immune complex; ICGN, immune complex glomerulonephritis; MGN, membranous glomerulonephritis; MW, molecular weight; SPHN, slowly progressive Heymann nephritis.

reaching the end of their life span, they release intracytoplasmic ags into the circulation and are removed by specific non-pathogenic IgM aabs and digested into reusable peptides by mononuclear cells [45,46]. The specific non-pathogenic IgM aabs are cross-reactive [42,43]; they are able to remove native aags from the system thereby preventing toxic accumulation of cellular breakdown products or their modifications. They are also able to remove modified (chemically or otherwise) aags as well, thereby preventing the development of autoimmune diseases.

Barabas and colleagues have demonstrated:

- that increased IgM aab titres can be obtained in normal rats' sera, against the renal cortical ag rich nephritogenic ag, following injections of native rat kidney fraction 3 (rKF3) ag in an aqueous solution [48];
- that by ab information transfer, employing donor rats' derived rat anti-rat kidney fraction 3 (rarKF3) IgM ab and native rKF3 ag (rich in nephritogenic ag) in the form of IC [rKF3 ag X rarKF3 IgM ab] increased levels of specific IgM aabs, directed against the nephritogenic ag, can be obtained after injecting normal recipient rats with the IC [48];
- that injection of ICs composed of [rKF3 ag X rarKF3 IgM ab] at slight ag excess can result in increased IgM aab production against the nephritogenic ag in treated rats, allowing efficient removal of nephritogenic ags (both native and modified) from the system, thereby halting the production of renal tubular and glomerular injury causing pathogenic IgG aabs. This form of vaccination prevented the development of SPHN in rats injected with the nephritogenic ag in an adjuvant; and in rats with the chronic form of SPHN terminated immunopathological processes that would have otherwise maintained the autoimmune kidney disease [48] (Table 1).
- That the vaccination method we are describing is the third way of immunizing after active and passive immunizations. It is called MVT because every time we want to immunize there is a need for producing specific ags to be targeted and specific abs against the target ags. ICs made up of the native target ag and the physiologic IgM ab against the target ag will produce in the vaccinated host the same ab with the same specificity against the target ag as present in the inoculum [12-14,72]. The immunization method is specific and safe, imitating natural immune responses to occur in the vaccinated host to correct the inability or compromised ability of the immune system to produce powerful corrective therapeutic response(s).

Table 1: Downregulation/termination of an experimental autoimmune kidney disease – SPHN – by the implementation of the MVT.

Clearance/removal of released intracytoplasmic ags into the circulation – physiological events.	Initiation of an experimental autoimmune kidney disease SPHN by the modified nephritogenic ag – pathogenic events.	Termination of an experimental autoimmune kidney disease SPHN by the implementation of the MVT – regaining tolerance to self.
Clearance of released intracytoplasmic ags (modified and native) ↓ assisted in the removal by cross-reactive physiologic IgM aabs ↓ • preventing toxic accumulation of released intracytoplasmic ags; and • development of an autoimmune kidney disease.	When modified nephritogenic aags prevail ↓ only partial clearance of the modified aags are removed by cross-reactive IgM aabs and ↓ the remaining modified aags cause the autoimmune kidney disease by cross-reactive pathogenic IgG aabs resulting in ↓ • targeted injury of the BB of the renal proximal convoluted tubules causing the autoimmune kidney disease; and • targeted attack in the glomeruli causing ICGN.	To terminate autoimmune kidney disease causing processes ↓ removal of native and modified nephritogenic ags from the circulation is paramount; ↓ it can be achieved by the implementation of the MVT ↓ • in SPHN, IC composed of: [native nephritogenic ag X homologous anti-native nephritogenic target ag IgM ab] injected into rats with the disease increased the level of circulating IgM aabs targeting both native and modified nephritogenic ags; and assisted in their removal, from the circulation, prior to being digested into peptides by mononuclear cells.

A range of possible immunological events are depicted against normal and modified nephritogenic ags released into the circulation; and regained tolerance to self by the implementation of the MVT.

Abbreviations: aab: Autoantibody; aag: Autoantigen; ab: Antibody; ag: Antigen; BB: Brush Border; IC: Immune Complex; ICGN: Immune Complex Glomerulonephritis; MVT: Modified Vaccination Technique; SPHN: Slowly Progressive Heymann Nephritis.

CONCLUSIONS

Barabas and colleagues have introduced the third vaccination technique – after active and passive immunizations – for the prevention and when present termination of certain exogenous and endogenous ag induced diseases [12-14,29,48,58,66,67]. The vaccine is introduced in an ab predetermined response format. The corrective immune responses are evoked by the immune system's natural abilities to initiate, and following continuous immunization, maintain the appropriate response, i.e., producing the same ab with the same specificity against the target ag that is present in the inoculum [12-14,72]. So far endogenous ag caused disorders such as autoimmune diseases and cancer have not been treated specifically to achieve cure. Medical interventions up until now have been used to achieve non-specific suppression of the immune system or the rapidly dividing cancer cells, thereby somewhat interfering with disease progression [4,30-34,73].

Prevention, progression and treatment of any disease depend upon the presentation of the disease causing ag to the cells of the immune system, whether it is exogenous or endogenous in nature. We have observed in an experimental autoimmune disease – SPHN – that the immune system is continually bombarded by released nephritogenic ags from the renal proximal convoluted tubules' BB zone of cells and as a result specific IgM aabs are produced against them [38,40,74]. The role of the specific IgM aabs is to assist in the removal of the released nephritogenic ag from the system, thereby preventing its toxic accumulation and possible chemical alteration which could, if allowed to stay in the system long enough, cause an autoimmune disease. The released aags, after being removed by the specific IgM aabs, are digested into small molecular weight reusable peptides by mononuclear cells [45,46,75].

We have shown that in order for an experimental autoimmune disease called HN or SPHN to occur, the native ag, i.e., the nephritogenic ag, has to be modified chemically or otherwise; because only the modified aag can induce the production of pathogenic autoimmune disease causing IgG aabs in genetically susceptible strain of rats [39]. Once such aabs [27,38,76,77] are produced, the target ag in the BB region of the proximal convoluted tubules is damaged causing the autoimmune disease (primary injury by the pathogenic IgG aab) with consequent release of the nephritogenic ag into the circulation and urine. The released aag, by contributing to IC deposition in the glomeruli, together with pathogenic IgG aabs directed against the nephritogenic ag in the presence of complement, caused MGN (secondary injury by the pathogenic IgG aab) [40] [exacerbation]. In the meantime, the released nephritogenic ag contributed to the production of elevated IgM aabs which in turn, by removing both modified and native nephritogenic ags from the system, downregulated/terminated the autoimmune disease causing immunopathological processes [27,38,40,48] [remission]. Without this inbuilt protective immune response most autoimmune diseases would progress rapidly damaging the target ag, causing functional and morphological injury in an organ.

During the chronic phase of the autoimmune disease it was observed that both pathogenic IgG and non-pathogenic IgM aabs were present in the circulation, directed against the nephritogenic ag [40]. The former maintained progression [exacerbation] and the latter aimed to downregulate/terminate the disease [remission]. Would we be able to initiate an increased non-pathogenic IgM aab response in SPHN rats against the native target ag (i.e., renal proximal convoluted tubules' nephritogenic ag), then we would be able to:

- remove both released native and modified native nephritogenic ags from the circulation; and thereby
- prevent further production of disease maintaining/progression causing pathogenic IgG aabs; and would
- regain tolerance to self;

Barabas and colleagues have worked out a new vaccination method which allows prophylactic and therapeutic interventions in rats with SPHN [11,48]. The vaccination technique is based on previous works showing that ICs used for immunization can enhance antibody response [78-84]. The third way of vaccination – after active and passive immunizations – is called MVT. It is eminently suitable to prevent and when present cure a pathogenic IgG aab induced and maintained experimental autoimmune kidney disease specifically, without noticeable side effects [11,48]. The vaccination is based on ab information transfer by administered ICs which are made up of the native target ag and non-pathogenic IgM ab directed against the native target ag. Vaccinating SPHN rats, ICs were made up of: [rKF3 ag X rarKF3 IgM ab] at ag excess. When the IC was injected into rats prior to the induction of SPHN, the level of circulating IgM aabs increased in the circulation and assisted in the elimination of both the modified and native nephritogenic ags and thus prevented the development of the kidney disease [11,48]. Animals injected with the same IC during the progressive phase of the kidney disease responded similarly with elevated specific IgM aab responses, which in turn, by removing the disease causing and contributing nephritogenic ags from the circulation, terminated the kidney disease [11,48].

Future possibilities for the employment of the MVT in humans are encouraging for preventing and when present terminating chronic disorders such as autoimmune diseases and cancer, specifically with minimal side effects.

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