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- This article is adapted from a presentation given by one of us (J.C.L.) as the John J. Bonica Lecture sponsored by the Eastern Pain Associa-98. Lecture sponsored by the Eastern Pain Associa-tion, the eastern regional chapter of the Ameri-can Pain Society. We thank Endo Laboratories for naltrexone and S. Hulsey for technical as-sistance. Supported by NIH grant NS-07628, a gift from the Brotman Foundation, and an NIMH training grant MH 15795 (G.W.T.).

In retrospect, such projects built on expectations of future energy requirements that failed to materialize within the time frames expected. Year after vear, long-range forecasts were revised down (14). The extent of the revisions challenged the basic understanding of energy demand. Planning projections increasingly fell short. The resulting uncertainty about the need for future facilities, combined with high interest rates, had a chilling effect on new investment in energy production and supply.

This uncertainty raises a concern for energy planning. In an expanding economy with stabilized energy prices, might not energy demand again begin to rise and return to past patterns of growth?

During the 10 years following the 1973 Arab oil embargo, significant changes took place in U.S. energy consumption (1, 2). After decades of steady growth, annual demand for energy leveled off and began to decline. Total energy consumption in 1983 was less than that in 1973, despite economic growth over this same period averaging 2.5 percent per year (3-5).

Trends in Industrial Use of Energy

In response to higher prices, occasional fuel shortages, and other factors, individuals, businesses, and institutions reduced energy use to minimize rising energy costs. Consumers, for example, purchased more efficient vehicles and drove them less (6), and homeowners insulated their homes and turned down thermostats (7, 8). Some industries modernized their plants and equipment; others had to shut down because of obsolescence (9-12). Economic growth slowed, and the economy underwent a transformation, moving away from energy-intensive activities (13). By 1983, energy consumption had fallen more than 30 percent below what long-established historical trends would have otherwise predicted.

Robert C. Marlay

Development plans of a number of

Summary. Industry's use of energy, accounting for approximately 40 percent of U.S. consumption, changed significantly after 1973. In 1982 industry consumed onethird less energy than trends established before 1973 would have predicted. Part of this reduction resulted from improvements in the efficiency of industrial process technologies. Most is attributed, however, to slower growth in industrial economic activity and unprecedented changes in the composition of industrial output away from industries that consume large amounts of energy.

energy supply projects were disrupted. Particularly hard hit were those with long lead times for implementation. Large power plants are visible examples, but similar fates were dealt to liquefied natural gas import facilities, synthetic fuel plants, deep wells for natural gas, certain coal mines and petroleum refineries, expansion plans for uranium enrichment, and others.

Then, because of the long lead times required for implementation, might not the energy facilities needed to meet the demand and nurture economic growth be years out of phase? A better understanding of energy demand would help to reduce this uncertainty and its associated risks, restore investor confidence in the legitimate need for certain energy supply facilities, and improve the infor-

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mation on which long-term energy planning and policy decisions are based.

In this article I examine the changing nature of energy demand in U.S. industry, identify a number of mechanisms of change, characterize their respective roles in reducing growth in industrial energy demand, and suggest a number of possible links between these mechanisms and more fundamental and underlying causes. Changing trends in measures of energy productivity specific to a variety of fuels are also examined. Such measures reveal the effects on energy use of improving the efficiency of industrial processes and of fuel substitution.



Between the end of World War II and 1973, industrial use of energy grew steadily at rates averaging between 2.7 and 3.6 percent per year, slightly less than the growth rate for industrial output in general. In Fig. 1, this growth and projections made in the 1970's are illustrated. By 1982, however, industry's use of energy was at its lowest level since 1967 and fully one-third less than what historical trends would have predicted. Yet throughout this period, industrial economic activity continued to expand, although at somewhat slower rates.

The amount of energy consumed by



Fig. 1. Industrial use of energy, 1947-1982. Historical trends represent growth rates of 2.7 to 3.6 percent per year. Projections to the year 2010, developed in the mid-1970's by the National Academy of Sciences (30) and considered low at the time (31), defined a broad range of plausible but vastly different assessments of long-term energy requirements.



Fig. 2. Reduced growth after 1973 in industrial use of (A) fuels and (B) electricity is attributed to (i) slower economic growth, (ii) changes in the composition of industrial output or shifts in output mix, and (iii) accelerated improvements in process efficiencies (15). The effects of each vary over time as shown by the bar charts at the top of the figure.

industry can be thought of as having three sources of variation. In the manufacture of any one kind of product, energy consumption varies with both the level of output and the efficiencies of the technologies of production. In the more general treatment of industry as a whole, however, there is an added complexity. This stems from the fact that there are more than 10,000 different kinds of products produced by industry. Some differ from others by as much as 100-fold in their intensity of energy use per unit of economic value. Further, the mix of these products can change quickly. New ones enter the marketplace as others drop out. Domestic products can be displaced by imports. Hence, when industry is viewed more generally as an economic aggregate, energy consumption depends additionally on the precise nature of that which is produced.

The changing patterns of industrial production, energy use, and energy productivity were examined for 472 industries in mining and manufacturing over a historical period from 1947 through 1982 (15). Data on production (output) were developed for each industry from quinquennial indexes of industrial production, published by the Bureau of the Census (16), and from monthly, quarterly, and annual indexes of industrial production, published by the Federal Reserve Board (17). Data were also developed for each industry on the costs and quantities of 21 forms of energy use and on a variety of economic statistics, including value of shipments, value added, value of year-end inventories, and the costs of capital, labor, and materials. Each industry was thus characterized as to its production history and its use of energy and economic resources, namely capital, labor, energy, and materials.

From the underlying data on output, aggregate measures of industrial production, weighted by selected energy and economic parameters, were constructed (18). Each measure was constructed to reveal a different aspect of industrial production, either intensive (relative measure) or consumptive (absolute measure) in its use of particular resources. An electricity-weighted aggregate measure of industrial production, for example, gives proportionally more weight to elements that consume large amounts of electricity. A value-added weighted measure, similar to that used by the Federal Reserve Board to monitor industrial economic activity, was constructed as a reference for use in making standard comparisons.

Finally, a number of indexes of indus-SCIENCE, VOL. 226 trial energy productivity were constructed by dividing fuel-specific energyweighted aggregate measures of industrial production by complementary measures of energy input (19). By defining energy productivity in this way, the effects on industrial energy demand of improvements in the efficiencies of process technologies could be measured independently of the effects, if any, of the changing level and composition of industrial output.

This distinction is important because it gives rise to different implications as to the underlying causes of changing energy demand. For example, the aluminum industry, at full production, accounts for roughly 10 percent of total industrial electricity use. In terms of its relative economic importance, however, it contributes less than one-half of 1 percent to total industrial value added.

Suppose, in the extreme, that domestic output of the aluminum industry fell from full production to zero. As a result, the amount of electricity used by the aluminum industry would also fall to zero. Total industrial demand for electricity, because of aluminum's large share, would fall by 10 percent. Industrial economic activity, however, as measured by value added, would fall by something on the order of only one-half of 1 percent.

Certain aggregate measures of industrial energy efficiency, such as energy use per constant dollar of industrial value added, would "improve" as a result, in this case by about 10 percent. Such improvements could easily be interpreted as promising signs of industry's improving energy efficiency. While this may be true in one sense, no fundamental improvements in the technologies of production were made at all. The apparent gains in efficiency observed at the aggregate level can be fully explained by a single change in the composition of industrial production. A large electricityconsumptive element dropped out, taking with it proportionally 20 times more energy than economic value.

Confusion concerning how much of reduced energy demand is due to improvements in process efficiency and how much is due to changes in the composition of output may be avoided by using a differently specified measure of energy productivity. In the example, an electricity-weighted, aggregate measure of industrial production, by virtue of the aluminum industry's large weighting factor, would drop by the same amount as electricity demand, that is, by 10 percent. In this construction, a ratio of 14 DECEMBER 1984



Fig. 3. Real prices of purchased energy to manufacturers (15). Price increases averaged 350 percent between 1972 and 1982. English unit prices in 1982 were \$31 per barrel of oil, \$4.20 per thousand cubic feet of natural gas, \$40 per ton of coal, and 4 cents per kilowatt hour of electricity.

electricity-weighted output over electricity input would show that process efficiency had remained unchanged, and that the drop in electricity demand was attributable solely to changes in the composition of industrial production.

By applying these measurement concepts to the assembled data and by analyzing changing trends in the variously weighted aggregate measures of industrial production and energy productivity, reduced growth in industrial energy demand after 1973 was found to be result of (i) slower growth in industrial economic activity, which depressed growth in energy demand by about 1.4 percent per year; (ii) accelerated improvements in process efficiencies, which depressed growth in demand by an additional 1.2 percent per year; and (iii) changes in the composition of industrial output or shifts in output mix, away from industries that consume large amounts of energy, which further depressed growth in demand by about 1.0 percent per year. The results of this work are shown separately for fuels and power in Fig. 2.

Improvements in energy productivity were significant, particularly with respect to industrial use of combustible fuels. Energy productivity increased more than 18 percent for all forms of energy combined and more than 30 percent for fossil and wood-derived fuels. The cumulative effect over the 9-year period from 1973 through 1982 of accelerated improvements in energy productivity, measured as a positive divergence from prior established trends, amounted to 18.9×10^{18} joules (10¹⁸ joules are roughly equivalent to 1 year's consumption of oil at the rate of 500,000 barrels per day), including direct use of electricity and the energy losses associated with its generation, transmission, and distribution. Similarly, the cumulative effect of shifts in output amounted to 17.4×10^{18} joules.

Changes in the composition of industrial production took place not only among industries consumptive and intensive in their use of energy but also among those intensive in their use of capital, labor, and materials. The long-established trend of labor-intensive industries toward declining relative economic importance accelerated. Industries intensive in their use of capital experienced slower growth, and those intensive in their use of materials posted major gains.

Materials-intensive industries are those characterized by relatively high costs (of total production costs) for purchased materials. Such industries are engaged primarily in the latter stages of processing and fabrication. They are often technologically sophisticated. Examples include a host of industries related to agricultural and food processing and others as diverse as aircraft manufacture, ready-mix concrete, computers and electronic equipment, and women's clothing.

While changes in the composition of industrial output occurred from year to year throughout the entire post–World War II period, both toward and away from certain industries, no change of like magnitude or duration was observed before 1970. These observations and the data on which they are based suggest that U.S. industrial production, in both its composition and use of energy, underwent and is perhaps still undergoing a transformation of unprecedented proportions, with implications for both longterm energy demand and a range of other socioeconomic issues.

Energy Prices and Other Causal Factors

The energy price increases of the last decade played an important and causal role in bringing about these changes. They motivated improvements in process efficiency, contributed to shifts in output mix, and likely had an ancillary role as well in slowing economic growth. Real prices to manufacturers (Fig. 3) increased more than fourfold for oil and natural gas and doubled for electricity and coal. While the prices of natural gas and electricity were still rising at the end of 1982, the price of coal stabilized at about one-third that of oil, reflecting coal's inherently lower economic value and higher cost of use.

In theory, as the price of energy rises faster than those of the other inputs to production, manufacturers will attempt to reduce their energy costs by eliminating waste and substituting, where possible, cheaper and alternative inputs. The result is improved energy efficiency. Manufacturers will also attempt to recover their increased energy costs by raising the prices of their products. But as the prices of energy-intensive products rise faster than those of other goods and services, consumers will buy less and substitute other products in their place. The result is a shift in the composition of output away from energy-intensive products. Finally, econometric evidence suggests that increased energy prices were responsible, at least in some part, for slower economic growth (20). Hence, energy prices may be linked to all three energy-reducing mechanisms.

The underlying causes of slower

growth and shifts in output mix, however, extend beyond energy price. In the energy-intensive steel industry, for example, reduced demand for steel output resulted from a variety of factors, of which the rising costs of energy was but one (21). High interest rates depressed demand for steel products by depressing the business activities of steel's major customers, including construction, automobile sales and manufacture, and investment in capital equipment and durable goods. Competition from industrial nations abroad challenged U.S. markets at unprecedented levels. Foreign steel increased its market share from 15 to 22 percent during this period. Although some claims of foreign subsidization were confirmed (22), most steel imports enjoyed fundamental competitive advantages. Products of high quality were produced by modern and efficient technologies at lower production costs, particu-



Fig. 4. Industrial use of fuels and power and related measures of energy productivity (15). Energy productivity, defined as a dimensionless index of energy-weighted industrial production, or output, divided by energy input (19), measures the combined effects of changing efficiency of process technologies and fuel substitution, independent of the level and composition of industrial production; BBL, barrels.

larly with respect to labor and energy. The difference in labor costs, for example, was identified by U.S. steelmakers to be the single most important factor contributing to the lack of domestic competitiveness and loss of market share (23).

The energy and economic developments after 1970 are complex and their relations to the level and composition of industrial production are not well understood. The increased price of energy, although an important factor reducing growth in energy demand, was not exclusive. Other factors, such as the prices of labor and capital, combined with outmoded and inefficient technologies, lagging innovation, and the internationalizing of domestic markets, also contributed to depressed growth in energy demand, perhaps as much as or more than the cost of energy.

Fossil Fuels and Wood Energy

Industry's use of coal, oil, natural gas, and energy derived from wood, and their associated measures of energy productivity (Fig. 4), also underwent a number of changes after 1970 (15).

Coal for all purposes other than making coke (Fig. 4A) declined throughout most of the 1970's. Manifested as increasing coal productivity (coal-weighted industrial output divided by coal input), this trend actually began in the mid-1960's coincident with increasing concerns over air quality and the growing availability of cheap natural gas. In the late 1970's, however, the decline in coal use slowed; some industries used less, but others used more. Case studies reveal that the increases were concentrated primarily in industries with production technologies adapted to particulate capture and sulfur absorption, such as the cement and lime industries (9, 24). The continued decline in coal use in industry at large, contrasted with these selected increases, suggests that federal, state, and local strictures concerning air quality, apart from their benefits, are impediments to the more general and expanded use of coal as an industrial fuel.

Coal used in the manufacture of coke (Fig. 4B) also declined, driven mainly by precipitously falling demand for steel. Capacity utilization in the steel industry fell to 38 percent in 1982, the lowest level since the Great Depression. Further, the efficiency of coke production improved markedly. This was achieved, in part, by investments in new facilities, but more importantly by the retirement of nearly half of the older, more polluting, and inefficient coke batteries.

Industrial use of wood as a source of energy (Fig. 4C) grew to a level of importance by 1980 surpassing that of all industrial coal used for nonmetallurgical purposes. Concentrated in the lumber and paper industries, increased use of wood after 1972 was the direct result of its substitution for other and more expensive fuels, primarily oil (24).

Before 1970, industrial use of natural gas (Fig. 4D) grew at rates ranging from 6 to 10 percent per year, but after 1973 these trends reversed abruptly. Although the price of natural gas in the mid-1970's was only half that of oil, federal price controls and rules governing the allocation of natural gas resulted in widespread curtailments for low-priority industrial users. These curtailments at times exceeded 30 percent of annually contracted amounts (25). New access to natural gas was forbidden to industrial customers throughout most of the 1970's, easing up only in the 1980's as natural gas became more available and as its price began to approach that of oil for the first time in 35 years.

Despite the fourfold increase in the price of oil, industrial use of this fuel continued to increase throughout the 1970's (Fig. 4E). As growth in industrial output slowed and oil use increased, petroleum energy productivity diverged negatively from the improving trends of the past. Industry not only used more oil but also used more oil per unit of output than historical trends would have predicted.

The efficiency by which industry used petroleum during this period undoubtedly increased in some areas as a result of oil's higher price. Yet overall, these gains were offset by increased use of oil in other areas. Oil was used as a substitute fuel for curtailed natural gas. Oil was also used as a substitute for coal, the expanded use of which was constrained for the reasons mentioned above. Finally, oil was used as a fuel of necessity in the case of expanding industrial economic activity because of the lack of alternatives.

Altogether, the changing trends in industrial energy productivity, which by construction screen out the effects of the changing level and composition of industrial output, reveal a remarkable interplay and responsiveness among the various fuels. In comparison with the trends before 1972, relative increases occurred in the use of heating coal, wood energy, and petroleum, while relative decreases occurred in the use of metallurgical coal and natural gas.

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Fig. 5. Industrially generated electrical power, including cogenerated power.

Although industry demonstrated extensive capability for substituting fuels, the increasing use of oil was somewhat counterintuitive, given its fourfold increase in price and the "energy crisis"– motivated pressures during the 1970's to use less. Within the constraints imposed by government regulation, however, such behavior was entirely consistent with economic expectations and the relative price movements shown in Fig. 3.

Collectively, these trends underscore the potentially powerful effects of certain federal policies, as well as the ineffectiveness of others. Regulations governing air quality and energy price controls significantly altered industrial use of coal and natural gas. The "oil back out" policies of the late 1970's, by contrast, were largely ineffective, defeated primarily by the lack of practical technological alternatives. Finally, policies aimed at encouraging increased industrial use of coal had little effect, at least in the near term. Except in limited applications, the expanded use of coal awaits the advent of cost-competitive, cleanburning, coal combustion technologies.

Electricity and Self-Generated Power

From 1947 through 1973, industrial use of electricity, including self-generated power, increased annually at rates far outpacing industrial economic growth. During the years of electrification before 1960, this growth often exceeded 10 percent per year. Growth continued over the next 15 years at about 5 to 7 percent per year. All the while, industry exhibited a strong and sustained preference for this form of energy, as evidenced by its increasing use of electricity per unit of output and its declining trend in energy productivity (Fig. 4F).

In the years following 1973, however, growth in electricity use slowed to about 2 or 3 percent per year, and the declining trend in electric energy productivity leveled off. This slowdown, illustrated in Fig. 2B, is attributed (15) to slower economic growth (which had a depressing effect on demand, about -1.7 percent per year); changes in the composition of industrial output away from electricity consumptive production (-0.8 percent per year); and a modest improvement in net energy productivity relative to historically declining trends (-0.5 percent per year).

The full extent of these effects, however, may not have been felt in utility sales of electricity to industry. The otherwise slowing growth in industrial electricity demand, in total, was offset in utility sales by about 0.8 percent per year by industry's sharply reduced use of selfgenerated power (Fig. 5) and its substitution with purchased power from the utilities.

In 1970, industry produced about 16 percent of its total requirement for electricity from its own generating plants. Although some of this power was from hydroelectric sources, 97 percent was derived from fossil fuels burned in conventional steam boilers. Self-generated power is not to be confused with cogenerated power. In industry, the latter is a small but burgeoning component of the former and involves the simultaneous generation of electricity and use of the waste heat from combustion.

By 1980, industrial use of self-generated power had fallen nearly 50 percent. Throughout the 1970's, there was a gradual shutdown of approximately 10 gigawatts of industrial generating capacity, roughly equivalent to ten of today's largest electric generating stations. The power no longer generated by industry was replaced by purchased power from the electric utilities, boosting utility sales by about 50 billion kilowatt hours per year by 1980.

Because of changing conditions, however, an opposite trend may be emerging, with corresponding implications for utility sales. The real price of oil, a major fuel of industrial generators, may stabilize or decline. Curtailments of natural gas, which had earlier shut down the industrial generators, ended in the early 1980's, and this fuel may become more available to industrial users. The price of replacement power purchased from the utilities, which had been a bargain at the regulated prices of the 1970's compared to the fourfold increase in the price of oil, may continue to rise. These developments, should they occur, combined with supportive regulatory treatment of cogeneration (26) and tax incentives (27) for new investment and, additionally, cogeneration, may cause a revival of industrially generated power of both the more traditional and cogenerated forms.

In summary, industrial demand for electricity purchased from central utilities was found to be measurably affected by a number of phenomena, two of which are not well studied-the changing composition of industrial production and the changing status of self-generated power. Because the collection of statistics on self-generated power was terminated in 1980 by the U.S. Department of Energy, the direction of more current trends concerning the latter is unknown.

Advanced Process Technologies

The potential for improving the energy efficiency of industrial processes is quite large (28). The average thermodynamic effectiveness of industrial energy use is estimated to be on the order of only 20 percent (29). Advanced technologies, particularly for certain energy-intensive processes, promise significant reductions in energy use and associated costs.

A sampling of these technologies includes continuous and thin-strip casting of steel; direct reduction of metal oxide ores; in situ metallurgical analysis of molten alloys; in-process sensors and hot inspection of products with computer scanning and pattern recognition technology; high-temperature materials, with long-range ordered atomic structures, having four times the strength of hightemperature steel; low-speed diesel cogenerators that achieve 85 percent thermal efficiency; advanced recuperators for improved utilization of waste heat: improved anodes and cathodes for aluminum smelting; membrane separation of process fluids as a substitute for evaporation and distillation; innovative process mediums, such as foam rather than water, for finishing and dyeing textile products; and others.

To the extent that energy is an important factor in the costs of production, such technologies offer potentially significant competitive advantages. Moreover, many are not simply improved versions of old practices but radically new concepts through which intermediate stages of processing are eliminated, improving productivity on several fronts simultaneously by reducing labor costs, improving quality, increasing yields, enhancing process flexibility and control, and reducing waste. Technologies already implemented, such as continuous casting of steel and textile foam finishing, are important factors increasing the competitiveness of these industries.

Apart from their economic benefits,

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advanced technologies affect energy demand in two countervailing ways. They reduce demand by improving efficiency and increase demand by increasing the competitiveness of and demand for products for which the energy is consumed to produce.

Conclusion

After 1973, industrial use of energy changed significantly. Higher energy prices brought improvements in energy efficiency, particularly with respect to the use of fossil fuels. These improvements reduced growth in energy demand, but only in part. Importantly, industrial economic growth slowed and the composition of industrial output shifted away from large energy-using industries. Slower growth and shifts in output mix together accounted for about two-thirds of the reduced growth in energy demand. The changing composition of industrial production was characterized primarily by the declining relative economic importance of industries intensive in their use of labor and energy, suggesting a role for advanced technologies aimed at improving industrial productivity.

The underlying causes of slower economic growth and shifts in the output mix were found to extend beyond energy price. Because the role of increased energy prices in reducing energy demand was not exclusive, the extent to which future demand would increase should energy prices decline is not clear. Nevertheless, these observations provide insights into the changing nature of industrial energy demand and suggest new modeling approaches.

The energy and economic developments of the 1970's changed virtually all previous trends in industrial use of specific fuels and power. Relative increases were observed in industry's use of petroleum, wood energy, and, in selected industries, coal, while relative decreases were observed for natural gas, coking coal, and, to a lesser extent, electricity. Finally, certain federal policies of this period strongly discouraged industrial use of natural gas and the expanded and more broadly based use of coal. Others aimed at encouraging the "back out" of oil were found to be largely ineffective in the industrial sector, at least in the near term. This was in part because of policies constraining industrial substitution of other fuels and more generally because of a lack of economic and environmentally acceptable alternative technologies.

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- 18. A factor-weighted, aggregate measure of industrial production, is given by

$$w_{j}^{I}(t) = \frac{\sum_{i=1}^{r} \frac{y_{i}(t)}{y_{i}(t_{o})} \cdot x_{ij}(t_{o})}{\sum_{i=1}^{t} x_{ij}(t)}$$
(1)

where I specifies the set of industries to be included in the aggregation, *j* defines the energy or economic parameter, or factor, to be used as the weight, $y_i(t)$ measures production (output) of industry *i*, belonging to the set of industries *I*, in time period *t*; $x_{ij}(t)$ is a quantity of energy or economic value of factor *j*, for industry *i*, in time eriod t; and t_0 is a reference time period

Industrial energy productivity, with respect to the use of a specific form of energy j, in time period t, for a given set of industries I, is a dimensionless ratio of j energy weighted output divided by i energy input diverse by divided by j energy input, given by

$$p_{j}^{I}(t) = \frac{\sum_{i=1}^{r} \frac{y_{i}(t)}{y_{i}(t_{o})} \cdot x_{ij}(t_{o})}{\sum_{i=1}^{I} x_{ij}(t)}$$
(2)

where the parameters are the same as those of Eq. 1, with the exception that the denominator is variable with respect to time. As applied, a substitution is made in the denominator, using aggregate time-series data on industrial energy consumption, $x_i^{l}(t)$, where

$$x_{j}^{\prime}(t) = \sum_{i=1}^{l} x_{ij}(t)$$
(3)

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RESEARCH ARTICLE

Influence of Clonal Selection on the **Expression of Immunoglobulin** Variable Region Genes

Tim Manser, Shu-Ying Huang, Malcolm L. Gefter

Vertebrates can produce a humoral immune response to a large number of different foreign antigens because B lymphocytes are able to synthesize immunoglobulins having many different antigen binding specificities. The diversity in structure of variable (V) regions, the antigen binding domains of immunoglobulins, results in diversity of antigen binding specificity. Each resting B cell in the lymphocyte population expresses immunoglobulin molecules with a single V region structure, and thus a single or limited number of binding specificities, as cell surface receptors. A subset of these cells are stimulated to grow and secrete antibody at the onset of an immune response partly as a result of foreign antigen being bound to surface immunoglobulin (1, 2).

Immunoglobulin V domains are formed by the association of heavy (H) and light (L) chain V region polypeptides. Molecular analysis of immunoglobulin genes in humans and mice show that transcriptionally active V genes are constructed in the DNA of the B cell lineage by fusion of gene segments that are separated in germ line DNA (3, 4). Segments of V genes are members of heterogeneous multigene families (5-9). Heavy chain variable region genes are formed by the fusion of three gene segments, V_H , D, and J_H (4, 6), whereas light chain variable region genes are formed from two segments, V_L and J_L (3, 5). The V region

structural diversity, directly encoded in germ line V gene segment families, is amplified as the result of (i) association of different combinations of segments during V gene formation (combinational diversity), (ii) variation in the joining sites of gene segments (junctional diversity) (5, 10), (iii) somatic mutation of assembled V region genes (11-15), and (iv) association of different V_H and V_L polypeptides during immunoglobulin assembly.

The genetic potential for V region diversity in mouse and man is therefore now well defined. It is not known, however, how much of this potential diversity is actually expressed as functional diversity, that is, diversity expressed in the V regions of B cell surface receptors that can interact with foreign antigen at the onset of an immune response (such as in the preimmune V region repertoire). Previous serological and antigen binding analyses of antibodies produced by B cells derived from unimmunized mice indicate that the number of different antigen binding specificities in the preimmune V region repertoire is extremely large ($\sim 10^7$) (16, 17) and that any single V region structure is likely to be expressed at a very low frequency in this repertoire (18, 19). It is generally assumed that combinational, junctional, and possibly mutational processes contribute to the diversity of V region structures in the preimmune repertoire. In fact, little is known concerning the relative contribution of these sources of diversity and whether or not functional restrictions to the random assortment and modification of V gene segments and their polypeptide products exist.

For several years we have used the immune response to para-azophenylarsonate (Ars)-protein conjugates in strain A mice as a model immune response. This response is characterized by the reproducible appearance in the serum of a family of antibodies containing V regions that bear serologically cross-reactive determinants (idiotype) and comprise an average of 50 percent of all hapten binding antibodies (20). Molecular characterization of monoclonal Arsbinding antibodies that express these idiotypic determinants (termed Id^{CR}), and the genes that encode them, has revealed that a single V_H gene segment $(V_H Id^{CR})$ participates in encoding all the $V_{\rm H}$ regions in these molecules (15). Amino acid sequences of the V_L regions of such molecules suggest that a single V_{L} gene segment, in combination with a single J₁ segment, encodes these polypeptides (V₁Id^{CR}) (21, 22). The dominant cross-reactive idiotypic family of antibodies elicited with Ars in strain A mice is therefore analogous to other major idiotypic families elicited in inbred strains by other antigens (23). The idiotype-bearing V regions expressed in these families are often encoded by small numbers of related $V_{\rm H}$ and $V_{\rm L}$ gene segments in combination with multiple, heterogeneous D and J gene segments. The $V_H Id^{CR}$ gene segment is, however, associated with both the J_H2 gene segment and an extremely homogeneous family of D region gene segments in the expressed V_H genes of hybridomas that synthesize Ars-binding Id^{CR}-bearing molecules (24, 25). Thus, a very limited amount of combinational diversity is ob-

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